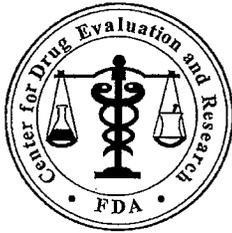


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

NDA 22-090

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**

Date: April 24, 2008

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Subject: Proprietary Name Review for Eovist

Drug Name(s): Eovist Injection (Gadoxetate Disodium)

Application Type/Number: NDA # 22-090

Applicant: Bayer Healthcare Pharmaceuticals, Inc.

OSE RCM #: 2008-478

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

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Eovist, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention does not object to the use of the proprietary name, Eovist, for this product.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Medical Imaging and Hematology Products to review the proposed proprietary name for its potential to contribute to medication errors. The proprietary name, Eovist, is evaluated to determine if the name could be potentially confused with other proprietary or established drug names.

1.2 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Primovist, for NDA # 22-090. The Division of Drug Marketing, Advertising and Communications found this name objectionable because it overstates the efficacy of the drug product by misleadingly implying it is superior to other treatments. Therefore, the Applicant provided Eovist and _____ as alternative names for this product.

1.3 PRODUCT INFORMATION

Eovist Injection (Gadoxetate Disodium), a gadolinium-based contrast agent, is indicated for use in magnetic resonance imaging (MRI) of the liver in adult patients. Each mL of Eovist Injection contains 181.43 mg gadoxetate disodium. The usual dose is 0.1 mL/kg to be administered undiluted as a single intravenous bolus at a rate of 2 mL/second. This product is available in 10 mL single use vials _____

2 METHODS AND MATERIALS

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

For the proprietary name, Eovist, the Medication Error Prevention Staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.2). The Medication Error Prevention Staff also conducts internal CDER prescription analysis studies (see 2.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

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

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.3). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.¹ FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Medication Error Prevention Staff 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.² We use the clinical expertise of the Staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the Medication Error Prevention Staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

2.1 SEARCH CRITERIA

The Medication Error Prevention Staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'E' when searching to identify potentially similar drug names, as 75% of the confused drug names

¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

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

reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.⁴⁵

To identify drug names that may look similar to Eovist, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (two, capital letter 'E' and lower case 't'), downstrokes (none), cross-strokes (one, lower case 't'), and dotted letters (one, lower case 'i'). Additionally, several letters in Eovist may be vulnerable to ambiguity when scripted, including the letter 'E' may appear as a 'C' or 'F'; lower case 'e' appear as a lower case 'i' or 'l'; lower case 'o' may appear as a lower case 'a' or 'u'; lower case 'v' may appear as a lower case 'n,' 'r,' or 'u' ; a lower case 'i' may appear as a lower case 'c' or 'e'; and a lower case 't' may appear as lower case 'f' or 'r'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Eovist.

When searching to identify potential names that may sound similar to Eovist, the Medication Error Prevention Staff searched for names with similar number of syllables (three), stresses (EE-oh-vist or ee-OH-vist), and placement of vowel and consonant sounds. Additionally, several letters in Eovist may be vulnerable to misinterpretation when pronounced including the letter 'v' may be misinterpreted as a 'b' or 'f' and '-st' may be misinterpreted as '-sc' or '-sk.' The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Prevention Staff was provided with the following information about the proposed product: the proposed proprietary name (Eovist), the established name (Gadoxetate Disodium), proposed indication (magnetic resonance imaging of the liver), strength (181.43 mg/mL), dose (0.1 mL/kg), frequency of administration (one time), route (intravenously), and dosage form of the product (injection packaged in a vial _____). Appendix A provides a more detailed listing of the product characteristics the Medication Error Prevention Staff general take into consideration.

Lastly, the Medication Error Prevention Staff also considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment, and the Staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

2.1.1 Data base and information sources

The proposed proprietary name, Eovist, was provided to the Medication Error Prevention Staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Eovist using the criteria outlined in 2.1. A standard description of the databases used in the searches is provided in Section 6 (References). To complement the process, the Medication Error Prevention Staff 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, we review the United States Adopted Name (USAN) stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Medication Error Prevention Staff to gather CDER professional opinions on the safety of the product and the proprietary name, Eovist. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Medication Error Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

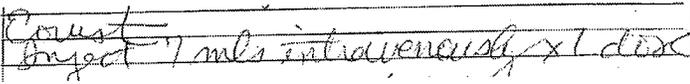
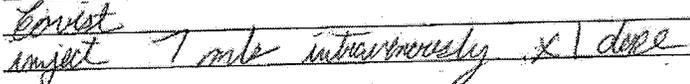
The pooled results of the Medication Error Prevention Staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.2 CDER PRESCRIPTION ANALYSIS STUDIES

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Eovist 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 a total of 122 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Eovist in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 122 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to the Medication Error Prevention Staff.

Figure 1. Eovist Study (conducted on April 9, 2008)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p>Inpatient Medication Order #1:</p> 	<p>Eovist Inject 7 mLs intravenously times one dose.</p>
<p>Inpatient Medication Order #2:</p> 	

2.3 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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.⁶ When applying FMEA to assess the risk of a proposed proprietary name, the Medication Error Prevention Staff seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name Eovist convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?” An affirmative answer indicates a failure mode and represents a potential for Eovist to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not

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

convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Medication Error Prevention Staff will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Medication Error Prevention Staff identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. Medication Error Prevention Staff identify a potential source of medication error within the proposed proprietary name. 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 another drug product.

In the event that we object to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, the Medication Error Prevention Staff will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while we will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Medication Error Prevention Staff will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, The World Health Organization, The Joint Commission and the Institute for Safe Medication Practices, having examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Medication Error Prevention Staff 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the Medication Error Prevention Staff believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If the Medication Error Prevention Staff objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. We are likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for the Medication Error Prevention Staff to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 DATA BASE AND INFORMATION SOURCES

The Medication Error Prevention Staff conducted a search of the internet, several standard published databases and information sources (see Section 6 References) for existing drug names which sound-alike or look-alike to Eovist to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 18 names were identified as having some similarity to the name Eovist.

Thirteen of the 18 names were thought to look like Eovist, which include: Aosept, Coriat, Covera, Emcyt, Enovid, Eovia, Eurax, Flovent, Ioversol, Levovist, Osmovist, Renovist, and

Tavist. One name (Magnevist) was thought to sound similar to Eovist. Four names (Eovist, Evamist, Evista, and Urovist) was thought to look and sound similar to Eovist.

A search of the United States Adopted Name stem list on March 24, 2008 identified no USAN stems within the proposed name, Eovist.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by the Medication Error Prevention Staff staff (see section 3.1 above), and noted no additional names thought to have orthographic similarity to Eovist. It should be noted the name, Levovist, was presented misspelled at the discussion as Levolist. Additionally, the reviewing Safety Evaluator did not present the names, Enovid, Eurax, and Flovent, to the panel as these names were provided by other members of the Medication Error Prevention Staff after the discussion concluded. However, the Safety Evaluator includes the three added names as well as the correctly spelled name, Levovist, in the Safety Evaluator Risk Assessment (see section 3.4)

The panel noted some potential sources for error at reviewing the product characteristics of Eovist presented at the discussion. The product has an unusual strength (181.43 mg/mL in 10 mL vials). The panel instructed the Safety Evaluator to verify the strength is consistent in the labels and labeling and the dosing instructions are clear. The dosing for Eovist is in terms of mL/kg rather than the more commonly seen term, mg/kg. The panel instructed the Safety Evaluator to verify the terms used for dosing by other imaging agents. Finally, the panel recommended the Safety Evaluator evaluate the calibration of the prefilled syringe to determine its potential to contribute to medication errors.

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

3.3 CDER PRESCRIPTION ANALYSIS STUDIES

A total of 30 practitioners responded. About one third of the participants (n=9) interpreted the name correctly as "Eovist," with correct interpretation occurring only in the written studies. One of the responses in Inpatient Medication Order #2 was Tavist, an existing drug name. The remainder of the responses misinterpreted the drug name. The misinterpretations occurred in the phonetic prescription study with the vowels in Eovist reported as 'Ee', or 'I' instead of 'E', 'a' or 'u' instead of 'o', and 'e' instead of 'i,' as well as misinterpreting the '-st' as an 'sc' or dropping the 't' at the end. In the written prescription studies, the letter 'E' was misinterpreted as an 'C' by two respondent, and a 'R' by two respondents. Also, the '-vi-' was misinterpreted as '-ru-' by twelve respondents. See Appendix A for the complete listing of interpretations from the verbal and written prescription studies.

3.4 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified an additional ten names thought to look or sound similar to Eovist and represent a potential source of drug name confusion. Nine of the ten names were thought to look similar including: Axert, Cenestin, Ionosol, Ionsys, Ioxilan, Livostin, Lonox, Lorcet, and Lunesta. The remaining name, Amvisc, was thought to sound similar to Eovist. As such, a total of 28 names were analyzed to determine if the drug

names could be confused with Eovist and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and /or phonetic similarity to Eovist, and thus determined to present some risk of confusion. Failure mode and effect analysis was then applied to determine if the potential name, Eovist, could potentially be confused with any of the 28 names and lead to medication errors.

This analysis determined that the name similarity between Eovist and the identified names was unlikely to result in medication errors for all 28 products. The first name, Eovist, was identified as the original proposed name for this product and has been trademarked in several foreign countries. Two of the 28 names identified (Coriat and Eovia) were determined not to be drug names (See Appendix C.) Two products (Levovist and Livostin) are available only in foreign countries. (See Appendix D.) Four names (Enovid, Osmovist, Renovist, and Urovist) are no longer marketed in the U.S. and have no generic equivalents available. (See Appendix E.) One name, Aosept, is an product line of contact lens solutions and devices. (See Appendix F.)

For nine of the 28 names (Amvisc, Axert, Cenestin, Covera, Flovent, Ionosol, Ioxilan, Lorcet and Lunesta), FMEA determined that medication errors were unlikely due to minimal orthographic and/or phonetic similarity to Eovist as well as they do not overlap in strength or dosage with Eovist (Appendix G).

For seven products available in only one strength (Emcyt, Eurax, Evamist, Evista, Ionsys, Lonox, and Tavist), FMEA determined that failure modes were unlikely to result in medication errors as these names have minimal orthographic and/or phonetic similarity to Eovist and also have multiple differentiating product characteristics to minimize the potential for medication errors despite the fact that these products and Eovist are only available in one strength which results in the strength being omitted when these products are ordered from wholesaler or pharmacy departments. (See Appendix H.) Although Eovist was misinterpreted as Tavist by one of the responders to the CDER prescription studies, Eovist's product characteristics, such as route of administration (intravenous), dosage form (injection) and specialized area of use in Radiology departments, minimize the potential for a medication error to occur.

The remaining two names, Ioversol and Magnevist®, include an overlap in dose with Eovist. However, analysis of the failure mode of these two product names did not determine the effect of this similarity to result in medication errors in the usual practice setting (Appendix I). Ioversol is one active of a combination product, Optiray®, used for CT scans and arteriograms. Magnevist has phonetic differences and is used for magnetic resonance imaging of the central nervous system, head, and neck.

The Safety Evaluator did not evaluate the labels for this review and thus was unable to determine the consistent use of the strength 181.43 mg/mL as recommended by the Expert Panel. However, the Safety Evaluator notes several other contrast agents, including Magnevist, which are dosed in terms of mL/kg. Thus, the Medication Error Prevention Staff believes healthcare practitioners in radiology departments will likely be familiar with the doses based on mL/kg like Eovist.

4 DISCUSSION

The results of the Proprietary Name Risk Assessment found that the proposed name, Eovist, has some similarity to other proprietary and established drug names, but the findings of the FMEA

indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Medication Error Prevention Staff believes that these limitations are sufficiently minimized by the use of an Expert Panel and the CDER Prescription Studies that involved 122 CDER practitioners.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Eovist, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the Medication Error Prevention Staff has no objections to the use of the proprietary name, Eovist, for this product. However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Medication Error Prevention Staff rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

Our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Medication Error Prevention Staff recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

We note from our review of the name Eovist, the product dosage forms include _____

We would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Janet Anderson, project manager, at 301-796-0675.

5.2 COMMENTS TO THE APPLICANT

The Medication Error Prevention Staff has no objections to the use of the proprietary name, Eovist, for this product at this time. We request that samples of the labels and labeling for Eovist

as well as a sample of the pre-filled syringe with graduations be provided for evaluation by the Division of Medication Error Prevention.

6 REFERENCES

1. ***Micromedex Integrated Index*** (<http://weblern/>)

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

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

3. ***Drug Facts and Comparisons, online version, St. Louis, MO*** (<http://weblern/>)

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

4. ***AMF Decision Support System [DSS]***

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

5. ***Division of Medication Error Prevention proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Medication Error Prevention Staff 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 and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and “Chemical Type 6” approvals.

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

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

8. ***US Patent and Trademark Office*** <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** (<http://weblern/>)

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

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

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

11. Natural Medicines Comprehensive Databases (<http://weblern/>)

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

12. Stat!Ref (<http://weblern/>)

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

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

**APPEARS THIS WAY
ON ORIGINAL**

APPENDICES

Appendix A:

The Medication Error Prevention Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Medication Error Prevention Staff also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Prevention Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has led to medication errors. The Medication Error Prevention Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Prevention Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Medication Error Prevention Staff will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, the Medication Error Prevention Staff also considers a variety of pronunciations that could occur in the English language.

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

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<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 Upstrokes Downstrokes	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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

Appendix B:

CDER Prescription Study Responses

Inpatient Medication Order #1	Inpatient Medication Order #2	Voice Prescription
Eoust	Eovist	Euvis
Eovist	Tavist	Eoven
Eorust	Covist	Eavist
Eorust	Eovist	Eavist
Rorust	Eovist	Iovisc
Eorust	Eovist	
Eorust	Eovist	
Eovist	Eovist	
Eorust		
Eorust		

Eovist		
Eorust		
Eorust		
Corust		
Eorust		
Eovist		
Eorust		

Appendix C: Names identified as not being products.

Proprietary Name	Similarity to Eovist	What the name identifies.
Coriat	Look	Author's last name in a Medical Reference
Eovia	Look	French company which creates 3-D modeling software.

Appendix D: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Eovist	Country
Levovist	Look	Germany
Livostin	Look	Canada, New Zealand and others (product withdrawn from US market in 2004 with no generic equivalent)

Appendix E: Proprietary names discontinued or withdrawal from the market with no available generic equivalent

Proprietary Name	Similarity to Eovist	Year product removed from US market
Enovid®	Look	1988
Osmovist®	Look	1998
Renovist	Look	NDA #10-040 marketed at different strengths under other proprietary names (Reno-30, Reno-60, Renografin, and Cystografin)
Urovist	Look and Sound	1995

Appendix F: Proprietary names used for a product line

Proprietary Name	Similarity to Eovist	What the name identifies
Aosept	Look	Over-the-Counter contact lens cleaner solution and devices.

Appendix G: Products with no overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Eovist (Gadoxetate Disodium)		1814.3 mg/10 mL (181.43 mg/mL)	Usual dose: 0.1 mL/kg one time as an intravenous bolus.
Amvisc®	Sound	12 mg/mL and 16 mg/mL (0.5mL and 0.8 mL syringes)	One syringe at time of eye surgery.
Axert®	Look	6.25 mg and 12.5 mg	One tablet by mouth once then repeat in two hours, if needed.
Cenestin®	Look	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg and 1.25 mg	One tablet by mouth daily.
Covera®	Look	180 mg and 240 mg	One tablet by mouth at bedtime daily.
Flovent®	Look	44 mcg, 110 mcg, and 220 mcg	Two inhalations twice daily.
Ionosol®	Look	Ionosol T and Ionosol B (T and B are modifiers that distinguish the electrolyte content.)	intravenous bolus and infusions doses vary based on patients electrolyte and hydration status.
Ioxilan (established name for Oxilan®)	Look	300 (62%) and 350 (73%)	0.25 to 0.39 mL/kg based on procedure and patient characteristics.
Lorcet®	Look	5 mg/500 mg, 7.5 mg/650 mg and 10 mg/650 mg	one to two tablets every four to six hours.
Lunesta®	Look	1 mg, 2 mg and 3 mg	One tablet by mouth at bedtime.

Appendix H: Names of products with only one strength

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Other differentiating product characteristics (excluding dose and frequency)
Eovist (Gadoxetate Disodium)		1814.3 mg/10 mL (181.43 mg/mL)	Usual dose: 0.1 mL/kg one time as an intravenous bolus.	
Emcyt®	Look	140 mg	14 mg/kg/day rounded to the nearest capsule and divided into three or four doses each day.	Eovist's specialized area of use (Radiology), route of administration, dosage form, frequency of administration, indication for use, prescribers.
Eurax®	Look	10 %	Apply once, and repeat in 24 hours.	Eovist's specialized area of use (Radiology), route of administration, dosage form, indication for use, prescribers
Evamist®	Sound and Look	1.53 mg per spray	One to three sprays daily.	Eovist's specialized area of use (Radiology), route of administration, dosage form, frequency of administration, indication for use, prescribers.
Evista®	Sound and Look	60 mg	One tablet daily.	Eovist's specialized area of use (Radiology), route of administration, dosage form, frequency of administration, indication for use, prescribers
Ionsys®	Look	40 mcg per dose	Apply transdermal system, change daily or after 80 doses delivered.	Eovist's specialized area of use (Radiology), route of administration, dosage form, indication for use, prescribers,
Lonox®	Look	2.5 mg/0.025 mg	Two tablets four times daily	Eovist's specialized area of use (Radiology), route of administration, dosage form, frequency of administration, indication for use, prescribers
Tavist®	Look	1.34 mg	One tablet twice daily.	Eovist's specialized area of use (Radiology), route of administration, dosage form, frequency of administration, indication for use, prescribers

Appendix I: Potential confusing name with overlap in dose

Eovist (Gadoxetate Disodium)	1814.3 mg/10 mL (181.43 mg/mL)	Usual dose: 0.1 mL/kg one time as an intravenous bolus.
Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>Ioversol (active ingredient along with iodine in Optiray® products) 160, 240, 300, 320 and 350 (strengths of Optiray® are based on concentration of iodine)</p>	<p>Orthographic similarity: Beginning 'iove-' similar to 'eovi-' when scripted. Overlapping doses- 6 - 15 mL. Specialized area of use- Contrast media.</p>	<p>Orthographic differences in the names as well as use for different types of imaging minimize the likelihood of medication error in the usual practice setting. <i>Rationale:</i> Orthographic differences stem from the fact that Ioversol has more letters (eight vs. six) compared to Eovist providing added length. In addition, Eovist ends with a letter containing a cross stroke 't.' As Ioversol is one active ingredient of a combination product, the proprietary name, Optiray®, will likely be used to order this product for CT scans and arteriograms. Eovist is indicated for MRI of the liver in adults.</p>
<p>Magnevist® (gadepentetate dimeglumine) 469.1 mg/mL 5 mL, 10 mL, 100 mL</p>	<p>Phonetic Similarity: three syllables, third syllable '-vist'. Overlapping doses: 6 – 14 mL. Contrast agents used for MRI's</p>	<p>Phonetic differences in the names minimize the likelihood of medication error in the usual practice setting. <i>Rationale:</i> Phonetic differences stem from the fact Magnevist contains consonants in the first (m- and -g) and second (n-) syllables compared to Eovist which contains none. Agents used in MRI's of different regions of the body (Liver vs. CNS, head and neck)</p>

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