

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-290

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: July 31, 2008

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Subject: Proprietary Name, Label, and Labeling Review

Drug Name(s): AdreView (Iobenguane I 123 Injection)
2 mCi/mL at calibration time

Application Type/Number: NDA # 22-290

Applicant: GE Healthcare

OSE RCM #: 2008-716

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, AdreView, 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, we do not object to the use of the proprietary name AdreView for this product.

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

The results of the Label and Labeling Risk Assessment found that the presentation of the proposed proprietary name (AdreView) on the proposed container labels for the glass vials and lead shield appear to be vulnerable to confusion that could lead to medication errors. The primary area of concern involves the presentation of the proposed proprietary name on both the glass vial label and the lead shield label, specifically the design of the first capital letter 'A', the two colored font of the name and the capitalization of the fifth letter 'V' in AdreView. The Division a Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated, and provides recommendations in Section 6 that aim at reducing the risk of medication errors. (See Section 3.2).

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Medical Imaging and Hematology Products on May 1, 2008, for the assessment of the proprietary name, as well as container labeling for the 10 milliliter glass vial and the lead shield for AdreView.

1.2 REGULATORY HISTORY

The Applicant filed a 505(b)(2) application for AdreView in March 2008 for referenced listed drug product Iobenguane I-131 (NDA 20-084). While AdreView (Iobenguane I-123) is seeking approval in the U.S. market for the indication of detection of primary or metastatic pheochromocytomas and neuroblastomas, it is currently approved in several European countries for the indication of localization of neural crest tumors and the detection, staging and follow-up on therapy of neuroblastomas.

1.3 PRODUCT INFORMATION

AdreView (Iobenguane I 123 Injection) is a diagnostic radiopharmaceutical containing a radioiodinated benzylguanidine indicated as an imaging agent for the detection of primary or metastatic pheochromocytomas and neuroblastomas. AdreView is available as sterile solution for intravenous injection 74 MBq/mL (2 mCi/mL) with total activity of 370 MBq (10 mCi) and it will be supplied as 5 milliliters of solution in a glass vial with _____ Each vial is enclosed in a lead container of appropriate thickness. The recommended dose of AdreView is a 10 mCi (370 MBq) intravenous injection for adults and the pediatric patients less than sixteen years old weighing greater than or equal to 70 kilograms. For pediatric patients less than sixteen years old weighing less than 70 kg, recommended dose should be calculated according to patient body weight.

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AdreView should be stored at 20°-25°C (68°-77°F) and should be stored within the original lead container or equivalent radiation shielding.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error and Prevention's Medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Label and Labeling Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division 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

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, AdreView, 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, AdreView, the medication error staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). We also conducted internal CDER prescription analysis studies (see 2.1.2). When provided, external prescription analysis studies' results are considered and incorporated into the overall risk assessment, however, there were no external prescription analysis studies provided for this application.

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 2.1.3). 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. 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. We use the clinical expertise of the Medication error 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 considers 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

¹ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>.

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

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, we consider 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

2.1.1 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 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{4,5}

To identify drug names that may look similar to AdreView, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), capital letters ('A' and 'V'), downstrokes (none), cross-strokes (none) and dotted letters (one 'i'). We assessed the applicant's capitalization of the letter 'V' in the fourth letter position of the proposed proprietary name, considering the two probable orthographic presentations of the word, with a capital 'V', : (AdreView) and with a lower case 'v' (Adreview). This consideration draws on the probability that the name will not always be scripted as 'AdreView' but rather 'Adreview', by healthcare practitioners.

Additionally, several letters in AdreView may be vulnerable to ambiguity when scripted, including the capital letter 'A' may appear as capital letter 'O' or 'Ce'; lower case 'd' may appear as 'l' or 'cl'; lower case 'r' may look like lower case 'n' or 's'; lower case 'e' may look like lower case 'i', 'o' or 'l'; upper case letter 'V' may appear as upper case 'U' or 'W'; lower case 'i' may appear as 'e', 'l' or 'r'; and lower case 'w' may appear as lower case 'u', 'r' or 'n'. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to AdreView.

When searching to identify potential names that may sound similar to AdreView, the medication error staff search for names with similar number of syllables (3), stresses (AD-re-view or Ad-re-VIEW), and placement of vowel and consonant sounds. Phonetic consideration was also given to the pronunciations that include 'And' rather than 'Ad' and 'der' rather than 'dre'. 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 staff were provided with the following information about the proposed product: the proposed proprietary name (AdreView), the established name (Iobenguane I-123), proposed indication (an imaging agent for the detection of primary or metastatic pheochromocytomas and neuroblastomas),

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

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)

strength (2 mCi/mL or 74 MBq/mL), dose (10 mCi or 370 MBq) frequency of administration (one administration prior to imaging procedure), route (intravenous injection) dosage form (solution for injection). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the medication error 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 medication error staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and information sources

The proposed proprietary name, AdreView, was provided to the medication error 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 AdreView using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the medication error 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, the Medication error staff review the 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.

2.1.1.2 CDER Expert Panel Discussion

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

The pooled results of the medication error 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. As part of the Expert Panel Discussion, the group also provides handwriting samples of the proposed proprietary name along with other look-alike names identified by the panel and the Reviewing Safety Officer.

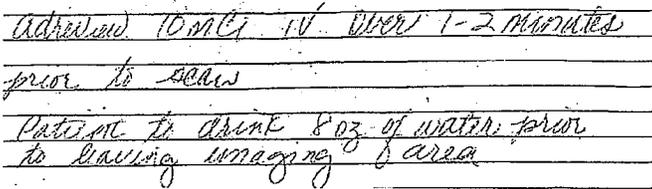
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2.1.2 CDER Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of AdreView 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 123 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 AdreView in handwriting and verbal communication of the name, inpatient medication orders are written, 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 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

Figure 1. AdreView Study (conducted on June 9, 2008)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u> N/A</p>	<p>Adreview 10 mCi IV over one to two minutes prior to scan. Patient is to drink eight ounces of water prior to leaving imaging area.</p>
<p><u>Inpatient Medication Order :</u> </p>	

2.1.3 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 Division seeks to evaluate the potential for a proposed name to be confused with

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

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 AdreView 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 AdreView to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the name possesses 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.

We will object to the use of proposed proprietary name when 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. We identify 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 staff identifies 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 and 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, we 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 we 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, World Health Organization, Joint Commission on the Accreditation of Healthcare Organizations and the Institute for Safe Medication Practices, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, we contend 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, we believe 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 we object 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 us 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.

2.1.4 Adverse Event Reporting System (AERS)

On May 16, 2008, we searched FDA Adverse Event Reporting system (AERS) to retrieve any medication errors since AdreView (Iobenguane Sulfate I-123) is currently a marketed product in European countries. The following criteria were used: MedDRA High Level Group Term (HLGT) 'Medication Errors' and the Preferred Term (PT) 'Pharmaceutical Product Complaint' with the established name Iobenguane, Iobenguane I-123 and AdreView.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The labels for the glass vials and lead shield communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁷

Because the Medication Error Prevention staff analyzes reported misuse of drugs, the staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. We use FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product, the review division forwarded the following revised label and labeling for our review on May 1, 2008 (See Appendix K and L images):

- Container Label for Glass Vial
- Container Label for Lead Shield
- Package Insert Labeling (no image)

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

The Division of Medication Error Prevention and Analysis conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to AdreView to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

practice settings. In total, sixteen names were identified as having some similarity to the name AdreView.

The sixteen names identified as having some look-alike or sound-alike similarity to the name AdreView. Fifteen of these names (Abacavir, Abreva, Aclovate, Adrenalin, Adrenam, Adrucil, Advair, Advicor, Andractim, Androvite, Astelin, Atazanavir, Atrovent, Otrivin, and Sclerosol) were thought to look like AdreView and one name (Myoview) was thought to sound like AdreView.

Additionally, the Division of Medication Error Prevention and Analysis did not identify any United States Adopted Names (USAN) stems in the name AdreView as of May 15, 2008.

3.1.2 Expert panel discussion

The Expert Panel reviewed the pool of names identified by the staff (see section 3.1.1. above) but did not identify any additional names with similarity to AdreView.

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

3.1.3 CDER Prescription Analysis Studies

A total of twenty-seven practitioners responded to the CDER prescription analysis studies, but none of the responses overlapped with any existing or proposed drug names. Approximately sixty-three percent (n=17) interpreted the name correctly as AdreView with correct interpretations occurring mostly in written studies. The remainder of the responses misinterpreted the drug name. Misinterpretations occurred primarily in the phonetic study, with 'Adre' being misinterpreted as 'Adj' by three respondents, 'Atra' by two respondents, 'Adri' by one respondent, and 'View' being misinterpreted as 'vue' by three respondents. Orthographic misinterpretations included 'Adre' being misinterpreted as 'Cidre' by two respondents, and interpreted as 'Andre' by three respondents. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Adverse Event Reporting System (AERS)

The FDA Adverse Event Reporting System (AERS) search conducted on May 16, 2008 did not retrieve any medication errors associated with AdreView (Iobenguane I 123 Injection).

3.1.5 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator found one additional name thought to look similar to AdreView and represent a potential source of drug name confusion. Alkaver was thought to have look-alike similarity to AdreView. As such, a total of seventeen names were analyzed to determine if the drug names could be confused with AdreView 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 AdreView, and thus determined to present some risk of confusion. Failure modes and effects analysis (FMEA) was then applied to determine if the proposed name AdreView could potentially be confused with any of the seventeen names and lead to medication error. This analysis determined that the name similarity between AdreView and the identified names was unlikely to result in medication errors for the seventeen product names.

Atazanavir, Myoview and Sclerosol were not considered further because they were assessed by the primary safety evaluator to lack convincing orthographic and/or phonetic similarities with AdreView. (See Appendix C).

Adrenam was not considered further because it is a foreign drug product marketed only in Germany, and thus determined by FMEA to pose minimal risk for error in the usual practice setting. (See Appendix D)

_____ and Otrivin were not considered further because they are drug products that are not available on the market because of _____ status or withdrawal by the Agency. (See Appendix E)

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For three names (Abacavir, Astelin, Atrovent) it was determined that medication errors were unlikely because the products do not overlap in strength or dosage with AdreView. (See Appendix F).

Advair and Advicor were not considered further because, although they have numeric overlap in strength or dose, they do not share overlap in any other pertinent product characteristics, and thus determined by FMEA to pose minimal risk for error in the usual practice setting. (Appendix H).

Four names (Abreva, Aclovate, Andractim and Androvite) shared overlap in single strength availability, however, were not considered further because they do not share overlap in any other pertinent product characteristics, and thus determined by FMEA to pose minimal risk for error in the usual practice setting. (Appendix I).

The remaining two names (Adrenalin and Adrucil) had some numerical overlap with AdreView in dosage or strength, however, analysis of the failure modes did not determine the effects of these similarities to result in medication errors in the usual practice setting. (Appendix J).

LABEL AND LABELING RISK ASSESSMENT

Review of the container labels identified areas of vulnerability that could lead to medication error, specifically with respect to the presentation of the proposed proprietary name.

3.2.1 Container Label for Glass Vial and Lead Shield

The proposed proprietary name is displayed in two colors.

The proposed proprietary name contains an unusual font for the first capital letter position 'A' in AdreView which distorts the appearance of the letter.

3.2.2 Package Insert Labeling

No comments at this time

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

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

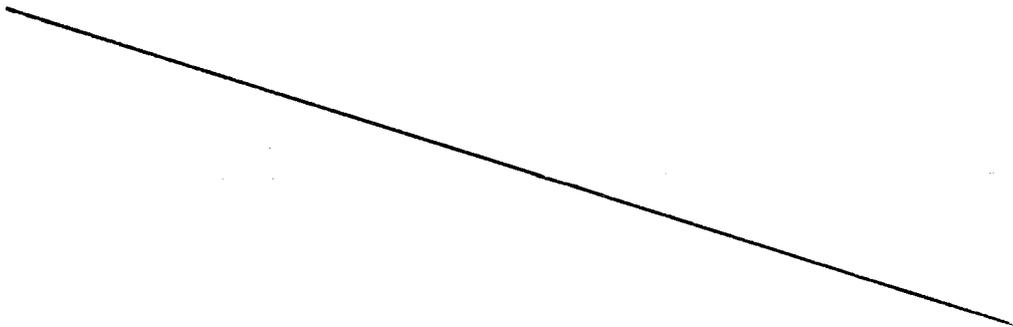
assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, we believe that these limitations are sufficiently minimized by the use of an Expert Panel and, in this case, the data submitted by the Sponsor from an independent proprietary name risk assessment firm, which included the responses of frontline practitioners.

However, 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.

4.2 LABEL AND LABELING RISK ASSESSMENT

The results of the Label and Labeling Risk Assessment found that the presentation of the proposed proprietary name on container labeling for the glass vial and lead shield appear to be vulnerable to confusion that could lead to medication errors.

4.2.1 Container Labeling for Glass Vial and Lead Shield



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5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, AdreView, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, we do not object to the use of the proprietary name, AdreView, for this product.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed container labeling for the glass vial and the lead shield introduce vulnerability to confusion that could lead to medication errors. We believe the risks identified can be addressed and mitigated prior to drug approval, and provide recommendations in Section 6 that aim at reducing the risk of medication errors.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

6.1.1 Proprietary name:

The Division of Medication Error Prevention and Analysis has no objections to the use of the proprietary name AdreView for this product.

If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review.

If the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

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

6.1.2 Label and Labeling:

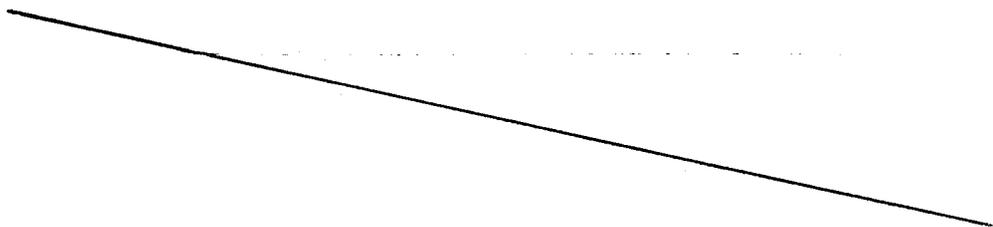
Based upon our assessment of the labels and labeling, the Division of Medication Error Prevention and Analysis has identified areas of needed improvement. We have provided recommendations in section 6.2 and request this information be forwarded to the Applicant.

6.2 COMMENTS TO THE APPLICANT

A. The Division of Medication Error Prevention and Analysis has no objections to the use of the proprietary name AdreView for this product. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for evaluation

B. Labels and Labeling

1. Container Labels for Glass Vial and Lead Shield



b(4)

2. Package Insert Labeling

No comments at this time.

7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous

reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

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

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

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

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

4. *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.

5. *AMF Decision Support System [DSS]*

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

6. *Division of Medication Errors and Prevention proprietary name consultation requests*

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

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

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

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

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

9. *United States Patent and Trademark Office <http://www.uspto.gov>.*

Provides information regarding patent and trademarks.

10. *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.

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

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

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

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

13. *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.

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

List contains all the recognized USAN stems.

15. *Red Book Pharmacy's Fundamental Reference*

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

16. *Lexi-Comp* (www.pharmacist.com)

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

17. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. We 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 staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* 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 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 (e.g., “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 staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, we 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, we also consider 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 – AdreView Study

INPATIENT	OUTPATIENT	VOICEMAIL
Adreveiw	Adre (Cidre) View	Adjavue
Adreview	Adre View	Adjurview
Adreview	Adreview	Adjuvue
Adreview	AdreView	Adraview
Adreview	AdreView	Adreview
Adreview	Adreview	Adrview (Adjeview?)
Adreview	AdreView	Atraview
Andreview	Adreview	Atravue
Andreview	Cidre View	
Andreview		

Appendix C: Drug names lacking convincing look or sound-alike similarities to AdreView

Proprietary Name	Similarity to AdreView
Atazanavir	Look-Alike
Myoview	Look-Alike
Sclerosol	Look-Alike

Appendix D: Drugs marketed in other countries

Proprietary Name	Country
Adrenam	Germany

Appendix E: Drugs not available on the market

Proprietary Name	Status	Date
Otrivin	Withdrawn by the Agency	September 1997

Appendix F: Drug names with no numerical overlap in strength and dose with AdreView

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
AdreView (Iobenguane I 123 Injection)		Specific Concentration: 74 MBq/mL (2 mCi/mL) Total Activity: 370 MBq (10 mCi)	Adult \geq 16 years old: 10 mCi (370 MBq) intravenously Pediatric Patients < 16 years old weighing \geq 70 kg: 10 mCi (370 MBq) intravenously Pediatric Patients weighing less than 70 kg: Recommended dose calculated according to body weight.
Abacavir (Abacavir Sulfate)	Look-Alike	300 mg Oral Tablets 20 mg/mL Oral Solution	Adults: 300 mg twice daily or 600 mg once daily Pediatrics: 8 mg/kg twice daily
Astelin (Azelastine Hydrochloride)	Look-Alike	0.125 mg Metered Nasal Spray	Adults: One to two sprays per nostril twice daily Children 5-11 years old: One spray per nostril twice daily
Atrovent (Ipratropium Bromide)	Look-Alike	0.021 mg/Spray; 0.42 mg/Spray Metered Nasal Spray	Two sprays per nostril 2-3 times daily

Appendix H: Drug names with numerical overlap in strength or dose but no similarities in primary product characteristics

Product name with potential for confusion	Strength	Usual Dose	Differentiating Product Characteristics
AdreView (Iobenguane I 123) Injection	74 MBq/mL (2 mCi/mL) 370 MBq (10 mCi)	Adult ≥ 16 years old: 10 mCi (370 MBq) intravenously Pediatric Patients < 16 years old weighing ≥ 70 kg: 10 mCi (370 MBq) intravenously Pediatric Patients weighing less than 70 kg: Recommended dose calculated according to body weight.	Route of administration is intravenous injection Dosage form is solution for intravenous injection Indication is diagnostic imaging agent for the detection of primary or metastatic pheochromocytomas and neuroblastomas
Advair (Fluticasone Propionate; Salmeterol Zinafoate)	Diskus: 0.1 mg/Inh; 0.05 mg base 0.25 mg/Inh; 0.05 mg base 0.5 mg/Inh; 0.05 mg base HFA: 0.045 mg/Inh; 0.021 mg base 0.115 mg/Inh; 0.021 mg base 0.23 mg/Inh; 0.021 mg base	Diskus: One inhalation 100/50 once daily or 250/50 twice daily HFA: Two inhalation twice daily	Route of administration is oral inhalation Dose form is inhalation powder diskus or aerosol Indication is for treatment of asthma
Advicor (Lovastatin / Niacin)	20 mg/500 mg; 20 mg/750 mg; 20 mg/1 gm; 40 gm/1 gm extended release oral tablets	20mg/500 mg once daily at bedtime; dose individualized based on targeted goals	Route of administration is oral Dose form is oral tablet form Indication is lipid-altering therapy

Appendix I: Drug names that overlap in single strength availability but no similarities in primary product characteristics

Product name with potential for confusion	Strength	Usual Dose	Differentiating Product Characteristics
AdreView (Iobenguane I 123) Injection	74 MBq/mL (2 mCi/mL) 370 MBq (10 mCi)	Adult ≥ 16 years old: 10 mCi (370 MBq) intravenously Pediatric Patients < 16 years old weighing ≥ 70 kg: 10 mCi (370 MBq) intravenously Pediatric Patients weighing less than 70 kg: Recommended dose calculated according to body weight.	Route of administration is intravenous injection Dosage form is solution for intravenous injection Indication is diagnostic imaging agent for the detection of primary or metastatic pheochromocytomas and neuroblastomas
Abreva (Docosanol)	10% Topical Cream	Apply to affected area. May use five times daily	Route of administration is topical Dosage form is topical cream Indication is for herpetic blisters/sores
Aclovate (Alclometasone Dipropionate)	0.05% Topical Cream or Topical Ointment	Apply thin film of Cream or Ointment to affected skin areas two to three times daily	Route of administration is topical Dosage form is topical cream or ointment Indication is for skin inflammation, pruritic dermatoses
Andractim (Dihydrotestosterone) Gel	2.5% Topical Gel	Apply to skin daily	Route of administration is topical Dosage form is topical gel Indication is male genital enhancement
Androvite (Dietary Supplement)	Dietary Supplement Oral Tablet	Take six tablets with meals; do not exceed six tablets a day	Route of administration is oral Dosage form is oral tablets Indication is a vitamin supplement for men

Appendix J: Drug names with potential for confusion due to overlapping product characteristics.

Failure Mode: Name confusion	Causes (could be multiple)	Effect
<p>AdreView (Iobenguane I 123 Injection)</p>	<p>74 MBq/mL (2 mCi/mL) 370 MBq (10 mCi)</p>	<p>Adult ≥ 16 years old: 10 mCi (370 MBq) intravenously Pediatric Patients < 16 years old weighing ≥ 70 kg: 10 mCi (370 MBq) intravenously Pediatric Patients weighing less than 70 kg: Recommended dose calculated according to body weight.</p>
<p>Adrenalin (Epinephrine) Injection Strength: 1:10,000 solution contains 0.1 mg epinephrine solution for intravenous, intracardiac, or endotracheal injection Dose: Hypersensitivity Reaction: 0.1 mg to 0.25 mg injected slowly. Neonates: 0.01 mg/kg repeated twenty to thirty minutes later Cardiac Arrest: 0.5 mg to 1.0 mg intravenously over five minutes Intracardiac: 0.3 mg to 0.5 mg</p>	<p>Orthographic similarities: Both names have the same begin 'Adre'.</p> <p>Numerical overlap in strength and recommended dose (0.1 mg versus 10 mCi)</p>	<p>Orthographic/phonetic differences in the names and variations in the setting of use minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i> The second portions of the names 'nalin' versus 'View' or 'view' vary orthographically. When AdreView is presented with a capital 'V' there is clear distinction in the appearance between the two names. Additionally, Adrenalin had an upstroke 'l' not present in AdreView, which differentiate the two words. Phonetically, Adrenalin has four syllables while AdreView has three syllables. The 'lin' sound in Adrenalin varies phonetically from the 'view' sound in AdreView.</p> <p>Administration of Adrenalin would likely occur in varying settings involving emergent treatment of acute hypersensitivity or cardiac arrest. Administration of AdreView, however, is limited to use within radiologic procedural department designated for SPECT imaging scans. The cumulative differentiation of product characteristics between AdreView and Adrenalin minimize the likelihood of medication error occurring at anytime during the drug ordering, preparation, dispensing, transport or administration phase.</p>
<p>Adrucil (Fluorouracil) Discontinued by generics available Strengths: 500 mg/10 mL; 1 gm/20 mL; 2.5gm/50 mL ; 5 gm/100 mL Solution for Intravenous Injection Dose: Intravenous: 300-500 mg</p>	<p>Orthographic and phonetic similarities: 'Adru' and 'Adre'.</p>	<p>Orthographic/ phonetic differences in the names as well as variations in units of measure and setting of use minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i> The endings of the two names vary in that the 'cil' in Adrucil has a distinctive upper case 'l' that is not present in the 'view' in AdreView. The two names differ phonetically, specifically in the pronunciation of the last syllables 'cil' versus 'view'.</p> <p>Variations in the units of measure (gram versus millicurie) differentiate the presentation of the strengths of Adrucil and AdreView. Setting of use for AdreView is specific to radiologic procedures (SPECT) scan, by personnel trained to handle radiopharmaceutical agents. Setting of use for Adrucil would likely be either an inpatient or outpatient oncology unit and would be administered by a broader range of health care professionals including registered nurses, nurse practitioners and oncology specialists. The cumulative differentiation of product characteristics between AdreView and Adrucil minimize the likelihood of medication error in the usual practice setting.</p>

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