

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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To: Rafael Dwaine Rieves, MD, Director
Division of Medical Imaging Products

Through: Melina Griffis, RPh, Team Leader
Denise Toyer, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Anne Crandall, PharmD., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Cysview (Hexaminolevulinate Hydrochloride) for Injection,
100 mg per vial

Application Type/Number: NDA 22555

Applicant/Applicant: Photocure ASA

OSE RCM #: 2010-346

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EXECUTIVE SUMMARY

Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Cysview, acceptable for this product. DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name, Cysview, must be re-evaluated.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Photocure ASA on February 10, 2010 for an assessment of the proposed proprietary name, Cysview, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

1.2 PRODUCT INFORMATION

Cysview is a diagnostic imaging agent indicated for photodynamic blue light cystoscopy performed with Karl Storz Photodynamic Diagnosis (PDD) system, as an adjunct to white light cystoscopy in the detection of non-muscle invasive papillary cancer of the bladder. The usual dose is 50 mL of reconstituted Cysview solution instilled into the bladder via catheter and retained in the bladder for approximately one hour before evacuation. Cysview will be available in a kit, which will include 100 mg of Cysview powder (as Hexaminolevulinate hydrochloride) in a 10 mL vial and 50 mL of solvent to dissolve the powder.

1.3 REGULATORY HISTORY

A previously proposed proprietary name for this product, Hexvix, was found to be unacceptable (OSE review # 2009-1599) [REDACTED] (b) (4). DMEPA also provided comments to the Applicant with respect to the proposed product label and labeling in OSE review # 2009-1501.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Cysview.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘C’ 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.^{1,2}

¹ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

² Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

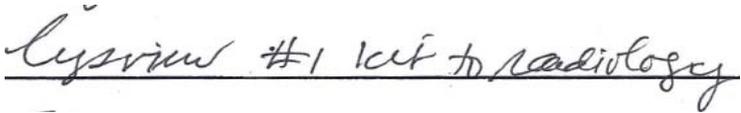
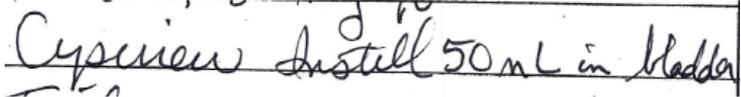
To identify drug names that may look similar to Cysview, the DMEPA staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (one, capital letter ‘C’), down strokes (one, ‘y’), cross strokes (none), and dotted letters (one, ‘i’). Additionally, several letters in Cysview may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Cysview.

When searching to identify potential names that may sound similar to Cysview, the DMEPA staff search for names with similar number of syllables (2), stresses (CYS-view or cys-VIEW), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can be misinterpreted (See Appendix B). The Applicant’s intended pronunciation, ‘sis-vyoo’, was taken into consideration, as it was included in the Proprietary Name Review Request. However, DMEPA also considers that names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient medication order and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Cysview Study (conducted on March 1 and March 2, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p data-bbox="272 1058 651 1087"><u>Inpatient Medication Order (#1):</u></p>  <p data-bbox="272 1213 1013 1247">Cysview #1 kit to radiology</p>	<p data-bbox="1159 1108 1349 1234">Cysview Number one kit To radiology</p>
<p data-bbox="272 1264 651 1293"><u>Inpatient Medication Order (#2):</u></p>  <p data-bbox="272 1457 1013 1470">Cysview Instill 50 mL in bladder</p>	<p data-bbox="1117 1264 1386 1339">Cysview Instill 50 mL in bladder</p>

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The database searches yielded a total of 16 names as having some similarity to the name Cysview.

All 16 names were thought to look like Cysview. These include: Cysteine, Lysodren, Lusedra, Cystagon, Adreview, Myoview, Azelaic, Apriso, Apexicon, Cystone, Zolyse, Cytovene, Cytosan, Azasan, Cipro IV, and Lysteda.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 2, 2010.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (see Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Cysview.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 33 practitioners responded in the prescription analysis studies. Five of the participants interpreted the name correctly as “Cysview”. Misinterpretations (i.e. ‘L’ confused for ‘C’, ‘view’ confused with ‘uin’, ‘rin’ ‘ron’ or ‘ren’) occurred in the written studies and misinterpretation (i.e. ‘Cys’ confused for ‘Sis’ or ‘Sys’ and ‘view’ confused for ‘bue’, ‘tu’ and ‘pue’) occurred in the spoken studies. One respondent misinterpreted the name Cysview for a currently marketed medication, Lupron, therefore the name was added to the risk assessment. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS (DMIHP)

3.4.1 Initial Phase of the Review

In response to the OSE e-mail on March 11, 2010 DMIHP did not forward any comments or concerns on the proposed proprietary name at the initial phase of the review.

3.4.2 Midpoint of the Review

On March 30, 2010 DMEPA notified the Division of Medical Imaging and Hematology Products via e-mail that we had no objections to the proposed proprietary name, Cysview. Per e-mail correspondence from DMIHP on April 26, 2010 they indicated that they concur with our assessment of the proposed proprietary name, Cysview.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified three additional names; Cystex and Lyrica were thought to look similar to Cysview and Synvisc was thought to sound similar to Cysview. Thus, a total of 20 names were evaluated for their potential similarity to Cysview.

Two of the 20 names, Cystone and Zolyse, were eliminated from further evaluation for the following reasons; 1) Cystone is a foreign drug and not marketed in the United States and 2) Zolyse is discontinued and not available as a generic.

The remaining 18 names were analyzed further to determine if the drug names could be confused with Cysview and if the drug name confusion would likely result in a medication error in the usual practice setting.

4 DISCUSSION

Cysview is the proposed proprietary name for Hexaminolevulinic Hydrochloride for Injection. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Medical Imaging Products concurred with the findings of the promotional assessment.

4.2 SAFETY ASSESSMENT

Twenty names were identified as being orthographically and/or phonetically similar to the proposed name Cysview. No other aspects of the name were identified as additional sources of error. Two of the twenty names were eliminated from further analysis at the initial screening.

Failure Mode and Effects Analysis was applied to determine if the proposed name, Cysview, could potentially be confused with the remaining 18 names and lead to medication errors. This analysis determined that the name similarity between Cysview and the identified names was unlikely to result in medication errors with any of the 18 products identified for the reasons presented in Appendices F through H.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Cysview, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Cysview, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In 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. Furthermore, if the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Catherine Carr, OSE Project Manager at 301-796-2311.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Cysview, and have concluded that the name is acceptable. The proposed proprietary name, Cysview, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you. If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

6 REFERENCES

1. ***Micromedex Integrated Index*** (<http://csi.micromedex.com>)

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

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

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

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

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

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 Errors Prevention and Analysis proprietary name consultation requests***

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

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

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

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

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

USPTO provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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 trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

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

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it 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>)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.⁵ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products

³ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁴ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

⁵ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA 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 even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies 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). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches 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 the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use 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 DMEPA staff review the USAN stem list to determine if any USAN stems are present within the

proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff 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 primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA 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 the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, two inpatient medication orders are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 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 DMEPA.

4. Comments from the OND review Division or Generic drugs

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

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

- a. 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

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

suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in name, Cysview	Scripted may appear as	Spoken may be interpreted as
Capital ‘C’	A, L, or O	S or Z
lower case ‘y’	j or g	I or E
lower case ‘s’	r, n	Z or C
lower case ‘v’	r, s, n	b or f
lower case ‘i’	e	silent
lower case ‘e’	i	silent
lower case ‘w’	vv or m	U

Appendix C: FDA Prescription Study (3/1 and 3/5) Responses.

Inpatient Medication Order (#1)	Voice Prescription (#1)	Inpatient Medication Order (#2)
Lysview	Cysview	Lysuin
Lysview	Cysview	Liprin
Lysview	Cispule	Lysiran
Lysview	Sispue	Lupron
Lysview	Sysbu	Lipcian
Lysview	?	Upiren
Cysview	Sistu	Lysian
Lysview	Cysview	Cypview
Lysview	Cystfu	Lysiren
Cysview		Cysrian
Lysview		

Appendix D: Drug is marketed in Foreign Country

Product Name	Status
Cystone***	Also identified in DARRTS as (b) (4)

Appendix E: Drug product discontinued, no generic available

Proprietary Name	Established Name
Zolyse	Chymotrypsin

Appendix F: Potential confusing names with no numerical overlap in strength or dose

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Cysview (Hexaminolevulinate hydrochloride)	NA	100 mg	100 mg in 50 mL of provided solvent, instilled in bladder
Apexicon (diflurasone diacetate)	Orthographic	0.05% topical ointment 0.05% topical cream	Apply as thin film one to three times daily depending on severity of condition
Lysine (L-Lysine)	Orthographic	312 mg, 334 mg, 500 mg, 1000 mg, oral tablet 500 mg oral capsule	312 mg to 1500 mg by mouth daily

Appendix G: Name confusion is prevented by the combination of stated product characteristics and/or orthographic differences as described

Product name with potential for confusion	Similarity to Cysview	Strength	Usual Dose	Differentiating product characteristics (Cysview vs. Product)
Cysview		100 mg/ 50 mL	100 mg in 50 mL of provided solvent, instilled in bladder	NA
Cysteine (Cysteine Hydrochloride Injection, USP)	Orthographic	0.5 g (50 mg/mL)	Intended for use only after dilution in Aminosyn. Each 10 mL of Cysteine should be combined with 12.5 g of amino acids given by central venous infusion.	<i>Route of administration</i> bladder instillation vs. intravenous infusion) <i>Volume of dose</i> 50 mL vs. 10 mL <i>Setting of Use</i> Cysteine is always administered with amino acids

Lysodren (Mitotane tablets, USP)	Orthographic	500 mg oral tablets	2 to 6 grams by mouth per day in divided doses, either 3 or 4 times a day. Doses are increased incrementally to 9 g to 10 g per day, doses can go as high as 18 to 19 g per day.	<u>Frequency of administration</u> once vs. 3 to 4 times daily <u>Route of administration</u> bladder instillation vs. oral <u>Dosage form</u> powder for solution vs. tablet
Lusedra (Fospropofol disodium)	Orthographic	35 mg/mL (total of 1,050 mg/ 30 mL) intravenous solution	Initial dose (weight based): 385 mg to 577.5 mg bolus injection Supplement dose based on response (weight based): 105 mg to 140 mg bolus injection	<u>Setting for use</u> preparation for imaging vs. sedation in operating room, patient must have supplemental oxygen <u>Route of administration</u> bladder instillation vs. bolus intravenous injection <u>Dose</u> 100 mg/50 mL one time vs. varying dose with supplemental doses based on patient response
Adreview (Iobenguane i 123)	Orthographic	370 MBq (10 mCi) per 5 mL	Adult dose: 370 MBq (10 mCi) intravenous injection Pediatric dose: 37 MBq (1 mCi) to 366.3 MBq (9.9 mCi) intravenous injection	<u>Setting of use</u> nuclear pharmacy vs. hospital pharmacy or imaging area <u>Safety requirements</u> none vs. radiation shield <u>Dose Designation</u> mL or mg vs. MBq or mCi
Azelaic acid	Orthographic	20% topical cream	Apply to affected area twice daily in the morning and evening	<u>Frequency of administration</u> (once vs. twice daily) <u>Route of administration</u> bladder instillation vs. topical application
Cytovene (Ganciclovir sodium)	Orthographic	500 mg powder for intravenous injection	Initial dose: 5 mg/kg intravenous infusion twice daily for 7 to 21 days then 6 mg/kg intravenous infusion 5 days per week	<u>Orthographic</u> - Cysview has one up-stroke, 'C', and no cross-strokes vs. Cytovene has a 2 upstrokes 'C' and 't' and cross-stroke with 't' - Cysview has one letter between the downstroke of 'y' and the string 'view' vs. Cytovene has two letters 'to' between the downstroke 'y' and the string 'vene' which makes the name appear lengthier <u>Frequency of administration</u> one time vs. twice daily <u>Dose</u> 100 mg/50 mL vs. weight based regimen

Lysteda (Tranexamic acid)	Orthographic	650 mg oral tablet	1300 mg by mouth twice or three times daily for 5 days during menstruation or 650 mg by mouth once daily during menstruation	<u>Frequency of administration</u> one time vs. two to three times daily <u>Route of administration</u> instilled via bladder vs. oral <u>Dosage form</u> powder for solution vs. tablet <u>Dose/strength</u> 50 mL vs. 1300 mg or 2 tablets
Cystex (Methena-mine, Sodium salicylate, Benzoic acid)	Orthographic	162 mg/ 162.5 mg/ 32 mg oral tablet	2 tablets 4 times daily with meals and at bedtime	<u>Frequency of administration</u> one time vs. four times daily <u>Route of administration</u> instilled via bladder vs. oral <u>Dosage form</u> powder for solution vs. tablet <u>Dose/strength</u> 50 mL vs. 2 tablets
Synvisc (Hylan polymers)	Phonetic	8 mg/mL, 2 mL syringe	16 mg weekly into the knee joint (intra-articular) injection for 3 weeks	<u>Frequency of administration</u> one time vs. weekly for 3 weeks <u>Route of administration</u> bladder instillation vs. knee joint
Cystagon (Cysteamine bitartrate)	Orthographic	50 mg, 150 mg oral capsule	100 mg to 500 mg by mouth every 6 hours	<u>Route of administration</u> bladder instillation vs. oral <u>Frequency of administration</u> one time vs. every 6 hours <u>Dosage form</u> powder for solution vs. capsule
Cytoxan (Cyclophosphamide)	Orthographic	25 mg, 50 mg oral tablets 500 mg, 1 g, 2 g powder for injection	Oral doses: 1 mg to 5 mg/kg/day for 60 to 90 days Intravenous dose: 10 to 50 mg/kg in divided doses over a period of 2 to 5 days or 3 to 5 mg/kg twice weekly	<u>Orthographic difference</u> -Cysview does not have any upstrokes after the first letter vs. Cytoxan has an upstroke due to the 't' -Cysview has no cross-strokes vs. Cytoxan has two cross-strokes with 't' and 'x' <u>Route of administration</u> bladder instillation vs. oral or intravenous <u>Frequency of administration</u> once vs. every day or two to five times a week
Azasan (Azathio-prine)	Orthographic	25 mg, 50 mg, 75 mg, 100 mg oral tablet	3 to 5 mg/kg by mouth daily, then reduce dose to 1 mg/kg to 3 mg/kg by mouth daily or 1 mg/kg to 2.5 mg/kg by mouth daily	<u>Orthographic differences:</u> The string of letters that ends the name Cysview, 'view' contains four letters with a dotted 'i' and also ends with 'w' which is wider letter vs. Azasan ends with the string 'san' with three letters and no dotted letter and ends with and a more narrow letter 'n' <u>Route of administration</u> bladder instillation vs. oral <u>Frequency of administration</u> once vs. every day

Lyrica (Pregabalin)	Orthographic	25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg oral capsule 20 mg/mL oral solution	50 mg to 200 mg by mouth three times daily 75 mg to 300 mg by mouth twice daily 25 mg to 150 mg by mouth once daily	<u>Route of administration</u> bladder instillation vs. oral <u>Frequency of administration</u> one time vs. one to three times daily <u>Dosage form</u> powder vs. capsule or oral solution
Cipro iv (Ciprofloxacin)	Orthographic	200 mg, 400 mg intravenous injection	200 mg to 400 mg intravenously every 4, 8 or 12 hours	<u>Frequency of administration</u> one time vs. two to six times per day <u>Dose</u> based on mL vs. based on mg, if by chance Cysview is ordered as 100 mg, it would not be confused with Cipro because Cipro is not available or recommended as a 100 mg dose
Lupron (Leuprolide acetate)	Orthographic	2.8 mL solution for injection	1 mg subcutaneously daily	<u>Route of administration</u> bladder instillation vs. subcutaneous <u>Frequency of administration</u> one time vs. every day

Appendix H: Similar name with multiple characteristics that help differentiate products

Failure Mode: Name Confusion	Causes (could be multiple)	Rationale
Cysview (Hexaminolevulinate hydrochloride)	Orthographic similarities Product characteristics	Factors that would prevent wrong drug selection.
Myoview (Tetrofosmin) Kit with 5 vials for use in the preparation of a technetium Tc99m tetrofosmin intravenous injection Dose is 5 mCi to 33 mCi, for stress and rest imaging test, two different doses given, 5 to 12 mCi followed by 15 to 33 mCi.	<i>Orthographic similarities include the following:</i> Same length (seven letters) Both contain ‘-view’ as the end. Both have ‘y’ as the second letter. Product characteristics that Cysview and Myoview share include: Both agents are considered imaging agents	Medication errors unlikely to occur in usual practice setting. <i>Rationale:</i> The risk for medication error is decreased by the following factors: 1. Orthographic differences -Beginning letters differ (‘C’ vs. ‘M’) 2. Product characteristics - Myoview Kit is used exclusively for Technetium preparation. These products are ordered exclusively from vendors that specialize in radioactive agents and stored in the Nuclear Pharmacy. The Myoview product (after preparation) must be shielded due to radiation emission and it must be assayed for total activity.

		<ul style="list-style-type: none">- Dose of Cysview is ordered in mL or possibly mg vs. dose of Myoview is ordered in mCi- Volume of syringe for Cysview is 50 mL vs. recommended doses of Myoview are 4 mL to 8 mL)-User radiation label must be filled out and attached to vial and syringe must be placed in metal shield or covering.- During post marketing surveillance, no errors have been reported that involved confusion with a radioactive agent and a non-radioactive agent. We suspect this is due to the distinct division of these two types of products which are ordered, stored and prepared by a select group of highly trained individual who solely deal with these radioactive agents.
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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22555	ORIG-1	PHOTOCURE ASA	HEXVIX

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/s/

ANNE CRANDALL
05/04/2010

MELINA N GRIFFIS
05/04/2010

DENISE P TOYER
05/05/2010

CAROL A HOLQUIST
05/05/2010