

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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22-470

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
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Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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To: Andrea Leonard-Segal, M.D., M.S.
Director, Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products

Through: Kellie Taylor, PharmD, MPH, Team Leader
Denise Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Zachary Oleszczuk, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Nexcede (Ketoprofen) 12.5 mg, Oral Soluble Film

Application Type/Number: NDA 22-470

Applicant/Applicant: Novartis

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EXECUTIVE SUMMARY

This review is written in response to a request from Novartis date June 16, 2009. Nexcede is the proposed proprietary name for Ketoprofen oral soluble film. 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. 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, Nexcede, conditionally 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 Division of Nonprescription Clinical Evaluation (DNCE) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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 is in response to a request from Novarits on June 16, 2009, for an assessment of the proposed proprietary name, Nexcede, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. DMEPA will assesses labels and labeling in a separate forthcoming review.

1.2 PRODUCT INFORMATION

Nexcede will be supplied as peppermint flavored or cinnamon flavored oral soluble film of 12.5 mg of ketoprofen. Nexcede is a nonsteroidal anti-inflammatory drug (NSAID) indicated for temporary relief of minor aches and pain due to headache, toothache, backache, minor pain of arthritis, common cold, muscular aches, menstrual cramps, and temporary reduction in fever. The active ingredient of Nexcede, ketoprofen, works by competitively inhibiting both cyclooxygenase (COX) isoenzymes, COX-1 and COX-2, by blocking arachidonate binding resulting in analgesic, antipyretic, and anti-inflammatory pharmacologic effects.

The dosing regimen for the Nexcede is to place one oral soluble film on top of the tongue and allow to dissolve every 4 to 6 hours as symptoms persist. If pain or fever does not get better in 1 hour, you may take 1 additional oral soluble film. With experience people may find they need two oral soluble films with the first dose. The oral soluble films will be individually wrapped in a foil cover and will be supplied in cartons of 20 oral soluble films.

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, 2.2, 2.3, and 2.4 identifies specific information associated with the methodology for the proposed proprietary name, Nexcede.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘N’ 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. ,

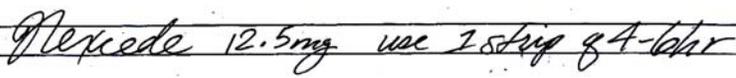
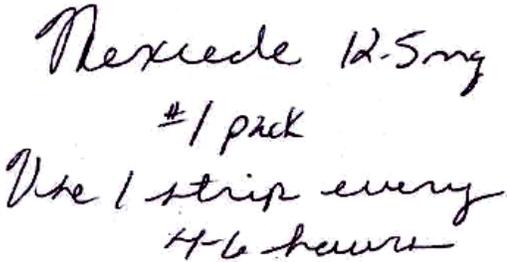
To identify drug names that may look similar to ‘Nexcede’, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (2, capital letter ‘N’ and lower case letter ‘d’), downstrokes (none), crosstrokes (1, lower case letter ‘x’), and dotted letters (none). Additionally, several letters in Nexcede 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 Nexcede.

When searching to identify potential names that may sound similar to Nexcede, the DMEPA staff searches for names with similar number of syllables (Two), stresses (NECK-seed or neck-SEED), and placement of vowel and consonant sounds. The Applicant’s intended pronunciation (nek seed) was also taken into consideration, as it was included in the Request for Proprietary Name Review. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Furthermore, 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 and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Nexcede Study (conducted on February 13, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Nexcede 12.5 mg #1 pack Use 1 strip every 4-6 hours</p>
<p><u>Outpatient Prescription:</u></p> 	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

2.4 COMMENTS FROM THE DIVISION OF NONPRESCRIPTION CLINICAL EVALUATION (DNCE)

The Division of Nonprescription Clinical Evaluation (DNCE) is contacted following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The Division of Nonprescription Clinical Evaluation is requested to concur/not concur with DMEPA's final decision.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 12 names as having some similarity to the name Nexcede.

Seven of the names were thought to look like Nexcede. These include Naxcel, Nexadron, Nexphen, Mexalen (b) (4), Mexate, and Nexavar. Two of the names were thought to sound like Nexcede. These include Neckweed and Nasex. The remaining three names were thought to look and sound similar to Nexcede; Nexcite, Excede, and Nexium.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 27, 2009.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1.1. above) and noted no additional names thought to have orthographic or phonetic similarity to Nexcede.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 23 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Nineteen of the participants interpreted the name correctly as “Nexcede,” with correct interpretation occurring in both the inpatient written studies (n=15) and the outpatient written studies (n=4). The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Nexcede. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by the Applicant, Addison Whitney identified and evaluated a total of 12 drug names (Nexium, Nexcare, Maxzide, Necon, Meridia, Neocate, Remicade, Excedrin, neomycin sulfate, Noxzema, Nexxus, and Nestea) that were thought to have some look-alike and/or sound-alike qualities and potential for confusion with Nexcede.

One of the 12 names (Nexium) was previously identified in DMEPA Staff searches and the Expert Panel Discussion.

3.5 COMMENTS FROM THE DIVISION OF NONPRESCRIPTION CLINICAL EVALUATION (DNCE)

DMEPA notified the Division of Nonprescription Clinical Evaluation via e-mail that we had no objections to the proposed proprietary name; Nexcede, on July 22, 2009. Per e-mail correspondence from the DNCE on insert July 24, 2008, they indicated they concur with our assessment of the proposed proprietary name, Nexcede and did not have any additional comments.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in 4 additional names (Refludan, Rifamate, Nixcreme, and Rifadin) which were thought to look or sound similar to Nexcede and represent a potential source of drug name confusion.

4 DISCUSSION

Neither DDMAC nor the review Division had concerns with the proposed name. DMEPA did not identify any issues with sound and look-alike concerns that would render the name objectionable.

Twenty-seven names were evaluated for their potential similarity to the proposed name, Nexcede. Nine of names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D).

Failure mode and effect analysis (FMEA) was then applied to determine if the potential name could potentially be confused with the remaining 18 names and lead to medication errors. This analysis determined that the name similarity between Nexcede was unlikely to result in medication errors with any of the 18 products for the reasons presented in Appendices E through K. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Nexcede, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Nexcede, for this product at this time. Additionally, DDMAC does not object to the proposed name, Nexcede from a promotional perspective.

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. 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.

5.1 COMMENTS TO THE DIVISION

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Darrell Jenkins, Project Manager, at 301-796-0558.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Nonprescription Clinical Evaluation (DNCE) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5.2 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Nexcede, and have concluded that it is acceptable.

If approval of the NDA is delayed beyond 90 days from the date of this review, the proprietary name will be re-reviewed prior to the new approval date.

If any of the proposed product characteristics are altered prior to approval of this NDA, 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.¹

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.

¹ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

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.² 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.³ 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 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.

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

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

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

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name 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, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of 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.⁴ 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:

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

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

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

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 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, Nexcede	Scripted may appear as	Spoken may be interpreted as
Capital ‘N’	‘M’	‘DN’, ‘GN’, ‘KN’, ‘MN’, or ‘PN’
Lower case ‘e’	‘a’, ‘i’, ‘l’, or ‘p’	‘A’, ‘I’, ‘ALL’, ‘U’, ‘O’ or ‘Y’
Lower case ‘x’	‘a’, ‘f’, ‘k’, ‘n’, ‘p’, ‘r’, ‘t’ or ‘v’	‘Z’ or ‘KS’
Lower case ‘c’	‘a’	‘Z’, ‘K’,
Combination lower case ‘ce’	‘a’	‘SU’
Lower case ‘d’	‘cl’	‘T’

Appendix C: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Nexcede	Nexcede	Nexced
Nexcede	Nexcede	
Nexcede	Nexcede	
Nexcede	Nexcede	
Nexcede	Nexiecle	
Nexcede	nexiede	
Nexcede	Nexiede	
Nexcede		

Appendix D: Names Lacking Orthographic and/or Phonetic Similarity.

Name
Nexadron
Nexphen
Nasex
Necon
Excedrin
Nestea
Nexxus
Noxzema
Neomycin

Appendix E: Proprietary or Established Names used only in Foreign Countries

Proprietary Name	Similarity to Nexcede	Country	Description
Mexalen	Look	Austria, Czech Republic, Honduras, Hungary	acetaminophen

Appendix F: Proposed proprietary names that were found unacceptable by DMEPA and the application for that product has been withdrawn or drug products that are discontinued and no generic equivalent is available

Proprietary Name	Similarity to Nexcede	Status and Date
(b) (4)		

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

Product name with potential for confusion	Similarity to Nexcede	Strength	Usual Dose
Nexcede		12.5 mg	12.5 mg orally every 4 to 6 hours as needed
Nexium	Look and Sound	Capsule: 20 mg and 40 mg Powder for Suspension: 10 mg, 20 mg, and 40 mg Powder for Injection: 20 mg and 40 mg	10 mg to 40 mg orally once daily or 20 to 40 mg by intravenous infusion once daily
Rifadin (Rifampin)	Look	Capsule: 150 mg and 300 mg Powder for Injection: 600 mg/vial	<u>Tuberculosis:</u> 10 mg/kg in a single daily administration not to exceed 600 mg once daily. <u>Meningococcal carriers:</u> Once daily for 4 consecutive days in the following doses: 600 mg (two 300 mg capsules) in a single daily administration. Or 600 mg every 12 hours for 2 days.
Meridia (sibutramine hydrochloride)	Look	Capsule: 5 mg, 10 mg, and 15 mg	5 mg to 15 mg orally once daily. Maximum dose is 15 mg per day

Appendix H: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Nexcede	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Nexcede vs. Product)
Nexcede		12.5 mg	12.5 mg orally every 4 to 6 hours as needed	
Naxcel (ceftiofur)	Look	Powder for injection 50 mg/mL	0.08 mg/lbs to 2.27 mg/lbs subcutaneously every 24 hours for 3 to 14 days depending on the species being treated	Dosage form (Soluble film vs. Powder for injection) Route (supralingual/oral vs. subcutaneous injection) Dose (12.5 mg vs. calculated based on weight (in lbs.) and species) Treatment population (humans vs. animals)
Refludan (lepirudin)	Look	Powder for injection 50 mg/vial	0.4 mg/kg body weight (up to 110 kg) slowly intravenously (eg, over 15 to 20 seconds) as a bolus dose, followed by 0.15 mg/kg body weight (up to 110 kg)/hour as a continuous intravenous infusion for 2 to 10 days or longer if clinically needed	Dosage form (Soluble film vs. Powder for injection) Route (supralingual/oral vs. intravenous injection/infusion)
Remicade (infliximab)	Look	Powder for injection: 100 mg/vial	3 mg/kg to 10 mg/kg given as an intravenous infusion given on day zero. Then 2 weeks and 6 weeks after that. Then every 4 to 8 weeks after that	Dosage form (Soluble film vs. Powder for injection) Route (supralingual/oral vs. intravenous infusion)

Appendix I: Products with overlap in strength, dose or achievable dose with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Nexcede	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Nexcede vs. Product)
Nexcede		12.5 mg	12.5 mg orally every 4 to 6 hours as needed	
Excede (cefitefur)	Look and Sound	Swine: 100 mg/ml Cattle: 200 mg/ml	Swine: 2.27 mg/lbs by intramuscular injection once Cattle: 3 mg/lbs by subcutaneous injection once	Dosage form (Soluble film vs. Injection) Route (supralingual/oral vs. subcutaneous or intramuscular injection) Dose (12.5 mg vs. calculated based on weight (in lbs.) and species) Treatment population (humans vs. cattle or swine)
Mexate (Methotrexate)	Look	25 mg/ml	Varies greatly depending on the disease ⁵ state and body surface area of the patient. In the treatment of neoplastic disease the maximum tolerated dose of methotrexate varies significantly from 80—900 mg/m ² IV without leucovorin rescue therapy and 900—30,000 mg/m ² IV with leucovorin rescue	Dosage form (Soluble film vs. Injection) Route (supralingual/oral vs. Intravenous or intramuscular) Dose (12.5 mg vs. calculated based on body surface area)

⁵ See Append K for a list of disease states and recommended dosages.

Product name with potential for confusion	Similarity to Nexcede	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Nexcede vs. Product)
Nexcede		12.5 mg	12.5 mg orally every 4 to 6 hours as needed	
Nix creme (permethrin)	Sound	1%	<p>Completely saturate the hair and scalp with Nix Crème Rinse. Apply Nix behind the ears and at the back of the neck.</p> <p>Leave Nix Crème Rinse on the hair for 10 minutes. Rinse with warm water.</p>	<p>Dosage form (Soluble film vs. Rinse)</p> <p>Route (supralingual/oral vs. topical to the scalp)</p> <p>Dose (12.5 mg vs. 1 application)</p>

Appendix J: Potential confusing name with numerical similarity in strength or dose

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
Nexavar (sorafenib) <u>Similarity to Nexcede:</u> Look <u>Dosage Form:</u> Tablets <u>Strength:</u> 200 mg <u>Usual Dose:</u> 400 mg orally twice daily	<p>Orthographic similarities: Both names contain the same number of letters (7), both names contain the same number of crosstrokes (1, lower case ‘x’) located in the same position (3rd letter), both names contain the same first 3 letters (‘Nex-’), and the 4th letter of each name may appear similar when scripted.</p> <p>Both products are only available in one strength (200 mg vs. 12.5 mg). Since both products are only available in one strength a prescriber would not have to include a strength when writing a prescription. Additionally, both products can share an overlapping frequency (twice daily) and route of administration (oral).</p>	<p>Although both products are only available in one strength, can share an overlapping frequency (twice daily), and overlapping route of administration (oral), the orthographic differences and difference in indications help to minimize the likelihood of confusion that could lead to medication error .</p> <p>Orthographically, both names contain a different number of upstrokes (2, capital ‘N’ and lower case ‘d’ vs. 1, capital ‘N’). Additionally, the endings of each name (‘-var’ vs. ‘-ede’) appear different when scripted.</p> <p>The indications of each product help to differentiate the two products. Nexavar is an oncology product for renal cell carcinoma and hepatocellular carcinoma and Nexcede is indicated for reduction in fever and pain. Oncology orders are usually more detailed than other medication orders. Since Nexavar is an oncology product any written order will most likely be detailed and specify a numerical dose (400 mg) a dosage forms (tablets) and/or an indication (renal cell carcinoma and hepatocellular carcinoma)⁶. If any of these components are included on a prescription it will help to minimize confusion between the two products.</p> <p>The orthographic differences between these two products provide for adequate differentiation of the two products and will help to minimize confusion that could lead to possible medication errors in the usual practice setting.</p>

⁶ American Society of Health-System Pharmacists (ASHP). ASHP Guidelines on Preventing Medication Errors with Antineoplastic Agents. *Am J Health-system Pharm.* 2002; 59:1648-86.

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Neckweed (brooklime)</p> <p><u>Similarity to Nexcede:</u> Sound</p> <p><u>Dosage Form:</u> Liquid</p> <p><u>Strength:</u> Unknown</p> <p><u>Usual Dose:</u> 1 teaspoon to 3 tablespoons orally 3 times daily</p>	<p>Phonetic similarities: Both names contain the same number of syllables (2), the beginning of both names my sound similar when spoken (“Neck- vs. ‘Nex-’) and the ending of each name may sound similar when spoken (‘-weed’ vs. ‘-cede’)</p> <p>Both products are only available in one strength (unknown vs. 12.5 mg). Since both products are only available in one strength a prescriber would not have to include a strength when writing a prescription. Additionally, both products can share an overlapping frequency (one to 3 times daily) and route of administration (oral).</p>	<p>The availability of each product will help minimize the likelihood of confusion that could lead to medication error for these two products. The proposed product, Nexcede will be available over-the-counter. Neckweed is an herbal supplement that does not appear to be available commercially. After searching the databases referenced in Section 6, references 1 through 16, DMEPA was unable to locate a commercially available product that contains only neckweed.</p> <p>However, Neckweed does appear in several databases listing the active moiety as brooklime, and listing several other common names such as Beccabunga, Mouth-Smart, Speedwell, Water Pimpernel, and Water Purslaneas that are also used for the active moiety of brooklime. Brooklime is herbal supplement that may be effective as a diuretic. Brooklime does appear in combination products, but none located specifically list neckweed.</p> <p>Only Natural Medicines Comprehensive Database listed a dose of neckweed (brooklime), however Natural Medicines Comprehensive Database failed to list a strength or availability of the product. Since neckweed does not appear to be commercially available and the alternate names of the active moiety of brooklime do not appear to be available in a single active ingredient product, it is unlikely that a prescriber would prescribe neckweed or another alternative name for this product.</p> <p>Since neckweed is unlikely to be prescribed and Nexcede will be available over-the-counter, the risk of confusion between the two products should be minimized</p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Nexcite (Carbonated Water, Sugar, Citric Acid, Damiana, Schizandra, Mate, Guarana, Caffeine, flovaoring, Ginseng, Sodium Benzoate, Colour)</p> <p><u>Similarity to Nexcede:</u> Look and Sound</p> <p><u>Dosage Form:</u> Liquid</p> <p><u>Strength:</u> Each 100 mL serving contains: Carbonated Water 93 g, Sugar 8.5 g, Citric Acid 0.2 g, Damiana 59 mg, Schizandra 58 mg, Mate 57 mg, Guarana 56 mg, Caffeine 30 mg, Flavoring 23 mg , Ginseng 18 mg, Sodium Benzoate 15 mg, and Colour 65 pg</p> <p><u>Usual Dose:</u> 1 bottle</p>	<p>Orthographic similarities: Both names contain the same number of letters (7), both names contain the same number of upstrokes (2, capital ‘N’ and lower case ‘t’ vs. Capital ‘N’ and lower case ‘d’) located in the same positions (1st letter and 3rd letter), both names contain the same first 4 letters (‘Nexc-’), the 5th letter of each name (‘i’ vs. ‘e’) may appear similar when scripted, and both names have the same last letter of the name (‘e’).</p> <p>Phonetic similarities: Both names contain the same number of syllables (2), both names have the same beginning (‘Nexc-’) and the ending of each name may sound similar when spoken (‘-ite’ vs. ‘-ede’)</p> <p>Both products are only available in one strength (see characteristic to the left vs. 12.5 mg). Since both products are only available in one strength a prescriber would not have to include a strength when writing a prescription. Additionally, both products can share an overlapping frequency (once) and route of administration (oral).</p>	<p>Although Nexcite and Nexcede have orthographic and phonetic similarities in addition to overlapping product characteristics, Nexcite is an energy drink and it is unlikely that a healthcare practitioner would prescribe this product. Since it is unlikely that Nexcite would be prescribed by a healthcare practitioner this should help to minimize the risk of confusion for these two products.</p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Rifamate (rifampin and isoniazid)</p> <p><u>Similarity to Nexcede:</u> Look</p> <p><u>Dosage Form:</u> Capsule</p> <p><u>Strength:</u> 300 mg rifampin and 150 mg isoniazid</p> <p><u>Usual Dose:</u> 2 capsule orally by mouth once daily</p>	<p>Orthographic similarities: Both names contain a similar number of letters (8 vs. 7), both names contain the same number of crosstrokes (1, lower case ‘t’ vs. lower case ‘x’), and the beginning of each name (‘Rifa-’ vs. ‘Nexc-’) may look similar when scripted.,</p> <p>Both products are only available in one strength (300 mg rifampin and 150 mg isoniazid vs. 12.5 mg). Since both products are only available in one strength a prescriber would not have to include a strength when writing a prescription. Additionally, both products can share an overlapping frequency (once daily) and route of administration (oral).</p>	<p>Although both products are only available in one strength, can share an overlapping frequency (once daily), and overlapping route of administration (oral), the orthographic differences help minimized the likelihood of confusion that could lead to medication error .</p> <p>Orthographically, both names contain a different number of upstrokes (3, capital ‘R’, lower case ‘f’ and ‘d’ vs. 2, capital ‘N’ and lower case ‘d’). Additionally, the endings of each name (‘-mate’ vs. ‘-ede’) appear different when scripted. Nexcede may also appears shorter than Rifamate when scripted.</p> <p>The orthographic differences between these two products provide for adequate differentiation the two products and will help to minimize confusion that could lead to possible medication errors in the usual practice setting.</p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Nexcare</p> <p><u>Similarity to Nexcede:</u> Look and Sound</p> <p><u>Dosage Form:</u> Product line for over-the-counter bandages, skin care products, cold sore treatments, diabetic skin care, and post surgical skin care for prevent of scars.</p> <p><u>Strength:</u> N/A</p> <p><u>Usual Dose:</u> N/A</p>	<p>Orthographic similarities: Both names contain the same number of letters (7), both names contain the same number of crosstrokes (1, lower case ‘x’) located in the same positions (3rd letter), both names contain the same first 4 letters (‘Nexc-’), the 5th letter of each name (‘e’ vs. ‘a’) may appear similar when scripted, and both names have the same last letter of the name (‘e’).</p> <p>Phonetic similarities: Both names contain the same number of syllables (2), and both names have the same beginning (‘Nexc-’).</p> <p>Both products are available over-the-counter, both products can have the directions for use as “use as directed”, and both products can have the quantity of dispense “#1 pack/box”.</p>	<p>Although both products are available over-the-counter, can share the same directions for use (use as directed), and the same quantity to dispense (1 pack/box), the orthographic and phonetic differences, in addition to the unlikelihood that a prescriber would order “Nexcare”, help minimized the likelihood of confusion that could lead to medication error .</p> <p>Orthographically, both names contain a difference number of upstrokes (2, capital ‘N’ and lower case ‘d’ vs. 1, capital ‘N’). Additionally, the endings of each name (‘-ede’ vs. ‘-are’) appear different when scripted.</p> <p>Phonetically, the second syllable of each name (‘-cede’ vs. ‘-care’) sound different when spoken.</p> <p>Additionally, it would be unlikely for a prescriber to simply order “Nexcare” since this is the name of a product line. The prescriber would have to specify if the patient is to receive bandages, skin lotions, cold sore treatments, or post operative scare kits. Since a prescriber would have to specify what type of Nexcare product a patient is to receive it is unlikely that Nexcare bandages or Nexcare cold sore treatment, for example would be confused for Nexcede.</p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Neocate (protein, carbohydrate, fat, sodium, and potassium)</p> <p><u>Similarity to Nexcede:</u> Look</p> <p><u>Dosage Form:</u> Powder</p> <p><u>Strength:</u> 13 g protein, 49.3 g carbohydrate, 19.1 g fat, 157 mg sodium, and 653 mg potassium per 100 g</p> <p><u>Usual Dose:</u> 5 scoops of Neocate in 5 ounces of water for each feeding</p>	<p>Orthographic similarities: Both names contain the same number of letters (7), both names contain the same number of upstrokes (2, capital ‘N’ and lower case ‘t’ vs. Capital ‘N’ and lower case ‘d’) located in the same positions (1st letter and 6th letter), both name contain the same number of crosstrokes (1, lower case ‘x’ vs. lower case ‘t’), both names contain the same first 2 letters (‘Ne-’), both names contain the same 4th letter (‘c’), and the ending of each name (‘-ate’ vs. ‘-ede’) may appear similar when scripted.</p> <p>Both products are available over-the-counter. Additionally, both products can share an overlapping directions for use (use as directed) and route of administration (oral).</p>	<p>Although both products are available over-the-counter, can have the same overlapping directions for use (use as directed), and share a route of administration, the orthographic difference in addition to the patient population should help to minimize confusion between the two products that could lead to medication errors in the usual practice setting.</p> <p>Orthographically, both names contain the same number of crosstrokes, however they appear in different positions (3rd letter vs. 6th letter).</p> <p>Additionally, the patient populations for these two products are distinct. Neocate has 5 different formulations of products (Neocate Infant, Neocate Nutra, Neocate DHA and ARA, Neocate One +, and Neocate Junior) that range in patient population from infant to 10 years of age. Nexcede is only proposed to be indicated in patients 16 years of age and older. The difference in patient populations should help to differentiate the products.</p> <p>Furthermore, prescribers would have to differentiate which Neocate product the patients are suppose to receive since there are 5 different formulations. The type of formula or supplementation formulation would help to differentiate orders for Neocate and Nexcede.</p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p>Maxzide (triamterene and hydrochlorothiazide)</p> <p><u>Similarity to Nexcede:</u> Look</p> <p><u>Dosage Form:</u> Tablets</p> <p><u>Strength:</u> 37.5 mg triamterene and 25 mg hydrochlorothiazide and 75 mg triamterene and 50 mg hydrochlorothiazide</p> <p><u>Usual Dose:</u> 1 or 2 tablets orally once daily</p>	<p>Orthographic similarities: Both names contain the same number of letters (7), both names contain the same number of crosstrokes (1, lower case ‘x’) located in the same position (3rd letter), both names contain the same number of upstrokes (2, capital ‘N’ and lower case ‘d’ vs. Capital ‘M’ and lower case ‘d’) located in the same positions (1st letter and 6th letter), the beginning of each name (‘Nex-’ vs. ‘Max-’) may look similar when scripted, and the endings for each name (‘-ede’ vs. ‘-ide’) may look similar when scripted.</p> <p>Both products may have a numerical overlap of 12.5 mg and 25 mg (12.5 mg vs. a half of tablet of 37.5 mg triamterene and 25 mg hydrochlorothiazide and two 12.5 mg oral soluble films vs. 1 tablet of 37.5 mg triamterene and 25 mg hydrochlorothiazide). Additionally, both products can share an overlapping frequency (once daily) and route of administration (oral).</p>	<p>Although the names have orthographic similarities and have overlapping product characteristics, the difference in strength, the usual presentation of dose and frequency, and the minimal documentation of confusion between names that begin with the ‘M’ and names that begin with the letter ‘N’ help minimize the risk of confusion between the two products.</p> <p>The strength is different for each product. Nexcede is a single strength product available as 12.5 mg and Maxzide is a combination product available in 2 strengths 25 mg/37.5 mg and 50 mg/75 mg. Since a strength would have to be included on a Maxzide prescription, the difference in strength should help differentiate the two products.</p> <p>Although both products share achievable or overlapping doses of 12.5 mg and 25 mg, a 25 mg dose for Nexcede would most likely include reference to the quantities as “2 films” or “12.5 mg x 2 films” since Nexcede will only be available as 12.5 mg oral soluble films. Additionally, a 12.5 mg dose for Maxzide would most likely be written in terms of an available strength of Maxzide. A dose of 12.5 mg for Maxzide would likely be written as “Maxzide 25 mg take ½ tablet daily”. Since the dose of each product is likely to be written in terms of an available strength of the product. The difference in strengths should help to differentiate the two products.</p> <p>Additionally, in the usual practice setting a written order for Maxzide would include the frequency of “once daily” or “qday”. It would be unlikely for any other frequency to be used since Maxzide is only dosed once per day. The usual dose for Nexcede is every 4 to 6 hours as needed. Although Nexcede could be dosed once day, it would be unlikely for a prescriber to order this frequency. More likely, a prescriber would write use as directed since this product can be taken on an as needed basis. Since Maxzide is only dosed once per day and the direction for use of “use as directed” would not be a usual frequency for this product and Nexcede would most likely have “every 4 to 6 hours” or “use as directed” as a frequency, the different frequencies may help to differentiate these products.</p> <p><i>(continued on the following page)</i></p>

Proprietary Name Nexcede (ketoprofen)	Strength Oral Soluble Film: 12.5 mg	Usual Dose: Allow one film to dissolve on tongue every 4 to 6 hours. If pain or fever dose not get better in 1 hour you may take 1 more film
Failure Mode: Name confusion	Causes (could be multiple)	Rationale
<p><i>(continued)</i></p> <p>Maxzide (triamterene and hydrochlorothiazide)</p> <p><u>Similarity to Nexcede:</u> Look</p> <p><u>Dosage Form:</u> Tablets</p> <p><u>Strength:</u> 37.5 mg triamterene and 25 mg hydrochlorothiazide and 75 mg triamterene and 50 mg hydrochlorothiazide</p> <p><u>Usual Dose:</u> 1 or 2 tablets orally once daily</p>	<p><i>(continued)</i></p>	<p><i>(continued)</i></p> <p>Furthermore, although the first letter of each name ('N' vs. 'M') can be confused for one another when scripted, there have been minimal documented cases of drug name pairs that have been confused for one another with this letter pair. The USP list of confused drug names does not list any name pair in which one name begins with an 'N' and the other name begins with an 'M'. The Institute of for Safe Medication Practices (ISMP) List of Confused Drug Names only lists one pair in which a name beginning with 'N' has been confused with a name beginning with the letter 'M'. Since reporting of medication errors is voluntary and under reported, a negative finding of names beginning with 'N' being confused for names that begin 'M' does not necessarily mean that the errors are not occurring, but only that the errors are not being reported.</p> <p>Although the names Nexcede and Maxzide do share orthographic similarities and overlapping product characteristics, the different strengths, different presentations of dose and frequency on a typical prescription, and the minimal documented confusion between names that begin with the letter 'N' and the letter 'M' help minimize the risk of confusion between this name pair that could lead to medication error.</p>

Appendix K: Mexate (Methotrexate) recommended doses⁷

Choriocarcinoma and similar trophoblastic diseases

Methotrexate is administered orally or intramuscularly in doses of 15 to 30 mg daily for a five-day course. Such courses are usually repeated for 3 to 5 times as required, with rest periods of one or more weeks interposed between courses, until any manifesting toxic symptoms subside.

Leukemia

Induction doses of 3.3 mg/m² in combination with 60 mg/m² of prednisone, given daily, produced remissions in 50% of patients treated, usually within a period of 4 to 6 weeks. Maintenance therapy is initiated, as follows: Methotrexate is administered 2 times weekly either by mouth or intramuscularly in total weekly doses of 30 mg/m². It has also been given in doses of 2.5 mg/kg intravenously every 14 days.

Mycosis fungoides (cutaneous T cell lymphoma)

Dosage in early stages is usually 5 to 50 mg once weekly. Dose reduction or cessation is guided by patient response and hematologic monitoring. Methotrexate has also been administered twice weekly in doses ranging from 15 to 37.5 mg in patients who have responded poorly to weekly therapy.

Osteosarcoma

The starting dose for high-dose methotrexate treatment is 12 grams/m².

⁷ Methotrexate injection, solution package insert found at Dailymed.com. June 30, 2009.

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/s/

ZACHARY A OLESZCZUK
08/28/2009

KELLIE A TAYLOR
08/28/2009

DENISE P TOYER
08/28/2009