

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761312Orig1s000

PROPRIETARY NAME REVIEW(S)

SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	6/3/2024
Responsible OND Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	BLA 761312
Product Name and Strength:	Lymphir (denileukin diftitox-cxdl) for injection 300 mcg/vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Citius Pharmaceuticals, Inc. (Citius)
Nexus NPNS ID #:	2024-236
DMEPA 2 Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD

1 PURPOSE OF REVIEW

This review is to reassess the proposed suffix, -cxdl, for BLA 761312, which was found conditionally acceptable on April 18, 2023^a, for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761312.

1.1 Regulatory History

FDA found the proposed suffix, -cxdl, conditionally acceptable for BLA 761312 on April 18, 2023^a. However, BLA 761312 received a Complete Response (CR) letter on July 28, 2023^b. Thus, Citius submitted a Class 2 Resubmission on February 13, 2024.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the previously proposed four-letter suffix, -cxdl, using the principles described in the applicable guidance^c.

Citius's proposed suffix, -cxdl, is comprised of 4 distinct letters. We note that the letters 'dl' within the suffix represent the medical abbreviation for 'deciliter'. We considered whether the inclusion of the letters 'dl' within the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

We determined that the proposed suffix -cxdl, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

^a Mena-Grillasca, C.M. Nonproprietary Name Suffix Review for denileukin diftitox-cxdl (BLA 761312). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 Apr 18. Nexus NPNS No.: 2022-128.

^b Richardson, N.C. Complete Response (BLA 761312). Silver Spring (MD): FDA, CDER, OND, DHMII (US); 2023 Jul 28.

^c Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

3 COMMUNICATION OF DMEPA 2 ANALYSIS

These findings were shared with OPDP. On May 22, 2024, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Hematologic Malignancies 2 (DHM 2) on June 3, 2024.

4 CONCLUSION

We find the suffix -cxdl acceptable and recommend the nonproprietary name denileukin diftitox-cxdl be used throughout the draft labels and labeling.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CARLOS M MENA-GRILLASCA
06/03/2024 02:11:43 PM

CHI-MING TU
06/03/2024 02:13:52 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	May 10, 2024
Application Type and Number:	BLA 761312
Product Name, Dosage Form, and Strength:	Lymphir (denileukin diftitox- cxdI) for injection, 300 mcg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Citius Pharmaceuticals, Inc. (Citius)
PNR ID #:	2024-1044725627
DMEPA 2 Safety Evaluator:	Ngoc-Linh Do, PharmD
DMEPA 2 Team Leader:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Associate Director for Nomenclature and Labeling:	Hina Mehta, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Lymphir, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the Reference section and Appendix A, respectively. Citius submitted an external name study, conducted by (b) (4)^a, for this proposed proprietary name.

1.1 REGULATORY HISTORY

We note that Ontak (denileukin diftitox) Injection was approved in 1999 under Eisai, Incorporated's application BLA 103767 for the treatment of adult patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor. We note that Citius is seeking an indication for BLA 761312 that is similar to the approved indication for Ontak (BLA 103767 under Eisai, Inc.) and Citius made reference to BLA 103767 and IND 110489. On January 8, 2014, Eisai, Inc, notified the Agency that Ontak production was being discontinued due to manufacturing issues. BLA 103767 is still in active status at the time of this review.

Eisai Inc, an authorized US agent for Citius, previously submitted the proposed proprietary name, (b) (4) *** under IND 110489 on February 24, 2022. However, on June 23, 2022, we found the name, (b) (4) *** unacceptable due to phonetic similarities and overlapping product characteristics with the proprietary name, (b) (4)^b.

Subsequently, Citius submitted the proposed proprietary name, Lymphir, for review on December 28, 2022 under BLA 761312. We found the name, Lymphir conditionally acceptable under BLA 761312 on March 23, 2023.^c However, the application received a complete response letter on July 28, 2023 due to product quality issues.

Thus, Citius submitted the name Lymphir, for review on February 13, 2024 as part of the Class 2 Resubmission for BLA 761312.

^a Proprietary Name Safety Summary for Lymphir (BLA 761312). (b) (4)
(b) (4) Available from: [\CDSESUB1\EVSPROD\bla761312\0042\m1\us\118-prop-names\118-proprietary-names.pdf](#).

^b Mena-Grillasca, C. Proprietary Name Review for (b) (4) *** (BLA 761312). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 JUN 23. PNR ID No. 2022-1044724459.

^c Iverson, N. Proprietary Name Review for Lymphir (denileukin diftitox-xxxx*) (BLA 761312). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 MAR 23. PNR ID No. 2022-1044724914.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on December 28, 2022^d and the prescribing information received on July 19, 2023^e.

Table 1. Relevant Product Information for Lymphir	
Intended pronunciation:	lim' feer
Nonproprietary name:	denileukin diftitox- cxdl
Indication:	For the treatment of adult patients with relapsed or refractory Stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy.
Dosage Form:	for injection
Strength:	300 mcg/vial
Route of administration:	Intravenous infusion
Dose and frequency:	9 mcg/kg/day administered as an intravenous infusion over 60 minutes on days 1 through 5 of a 21-day treatment cycle
How Supplied:	Supplied as a sterile, white, lyophilized powder for reconstitution in a single-dose vial containing 300 mcg denileukin diftitox- cxdl. Each carton contains one vial.
Storage:	Store in a refrigerator between 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze

2 DISCUSSION

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Lymphir.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Lymphir would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Lymphir. The Division of

^d Proprietary Name Safety Summary for Lymphir (BLA 761312). (b) (4)

Available from: <\\CDSESUB1\EVSPROD\bla761312\0042\m1\us\118-prop-names\118-proprietary-names.pdf>.

^e Proposed prescribing information for Lymphir (denileukin diftitox-xxxx*). Cranford (NJ): Full Applicant/Sponsor name; 2023 Ju 19. Available from: <\\CDSESUB1\EVSPROD\bla761312\0039\m1\us\114-labeling\114a-draft-label\11413-draft-labeling-text-clean.docx>.

Hematologic Malignancies 2 (DHM 2) concurred with the findings of OPDP’s assessment for Lymphir.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Lymphir.

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

There is no USAN stem present in the proposed proprietary name.^f

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Citius did not provide a derivation or intended meaning for the proposed proprietary name, Lymphir, in their submission. This proposed proprietary name, Lymphir, is comprised of a single word that contains the letters ‘-ir’ in the suffix of the name, which is the abbreviation for ‘immediate release’.

Although we typically discourage the inclusion of medical abbreviations in proprietary names, we note the letter strings ‘IR’ is a common letter strings in existing drug nomenclature (e.g., Advair, Humira, Levemir, etc.) and we are unaware of post-market reports of medication errors associated with these specific abbreviations through our routine surveillance. As the letter string ‘IR’ is located at the end of the name, we also evaluated the potential risk of misinterpreting the proposed proprietary name as “[drug name similar to Lymph] IR” and did not identify any names that would pose a risk for confusion.^g Therefore, in this case we do not object to the proposed proprietary name based on the inclusion of this medical abbreviation.

Lymphir does not contain any other components (i.e., a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

On March 22, 2024, the Division of Hematologic Malignancies 2 (DHM 2) did not forward any comments or concerns relating to Lymphir at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Eighty-seven (87) practitioners participated in DMEPA’s prescription simulation studies for Lymphir. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

^f USAN stem search conducted on April 27, 2024.

^g POCA search for ‘Lymph’ conducted on March 2, 2023.

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search^h identified seventeen (17) names with a combined score of $\geq 55\%$ or an individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified one name not previously analyzed. This name is included in Table 2 below.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

Table 2. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	1
Low similarity name pair: combined match percentage score $\leq 54\%$	0

2.2.7 SAFETY ANALYSIS OF NAMES WITH POTENTIAL ORTHOGRAPHIC, SPELLING, AND PHONETIC SIMILARITIES

Our analysis of the one name contained in Table 2 determined none of the names will pose a risk for confusion with Lymphir as described in Appendix E.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On May 10, 2024, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 2 (DHM 2).

3 CONCLUSION

The proposed proprietary name, Lymphir, is conditionally acceptable.

If you have any questions or need clarifications, please contact Cándido Alicea, PhD, OSE project manager, at (240) 402-8310.

^h POCA search conducted on April 26, 2024 in version 5.8.

3.1 COMMENTS TO CITIUS PHARMACEUTICALS, INC.

We have completed our review of the proposed proprietary name, Lymphir, and have concluded that this proprietary name is conditionally acceptable.

If any of the proposed product characteristics as stated in your submission, received on February 13, 2024, is altered prior to approval of the marketing application, the proprietary name must be resubmitted for review.

4 REFERENCES

1. *United States Adopted Names (USAN) Stems*

USAN Stems List contains all the recognized USAN stems, available at <https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems>.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved brand name and generic drugs; therapeutic biological products, prescription and over-the-counter human drugs; and discontinued drugs (see Drugs@FDA Glossary of Terms, available at <https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms>).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html>).

Purple Book

The Purple Book is an online database that contains information about biological products, including biosimilar and interchangeable biological products, licensed (approved) by the FDA under the Public Health Service (PHS) Act. See Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, available at <https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or>.

Division of Medication Errors Prevention and Analysis pending proprietary name requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis.

5 APPENDICES

APPENDIX A. FDA'S PROPRIETARY NAME RISK ASSESSMENT EVALUATES PROPOSED PROPRIETARY NAMES FOR MISBRANDING AND SAFETY CONCERNS

1. **Misbranding Assessment:** For prescription drug products, the Office of Prescription Drug Promotion (OPDP) assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by the Office of Non-Prescription Drugs (ONPD). OPDP or ONPD evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or ONPD provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. **Preliminary Assessment:** We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 3*. 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.ⁱ

*Table 3. Prescreening Checklist for Proposed Proprietary Name	
Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.	
Y/N	Is the proposed name obviously similar in spelling and pronunciation to other names?
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	Are there inert or inactive ingredients referenced in the proprietary name?
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	Does the proprietary name include combinations of active ingredients?
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	Is there a United States Adopted Name (USAN) stem in the proprietary name?
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.

ⁱ National Coordinating Council for Medication Error Reporting and Prevention. <https://www.nccmerp.org/about-medication-errors>. Last accessed 10/05/2020.

*Table 3. Prescreening Checklist for Proposed Proprietary Name	
Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.	
Y/N	Is this proprietary name used for another product that does not share at least one common active ingredient?
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	Is this a proprietary name of a discontinued product?
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, Cerner RxNorm, Purple Book, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score $\geq 70\%$.
- Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
- Low similarity: combined match percentage score $\leq 54\%$.

Using the criteria outlined in the check list (Table 4-6) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 4).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - o Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in

the confusion of drug names^j. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.

- o Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 5).
 - Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.
- c. FDA Prescription Simulation Studies: DMEPA also conducts prescription simulation studies using FDA health care professionals.

Four 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, verbal pronunciation of the drug name or during computerized provider order entry. 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 vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.
- d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND), Office of Generic Drugs (OGD), and/or Office of Pharmaceutical Quality (OPQ) for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-

^j Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the Safety Evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

Additionally, other review disciplines opinions such as OPQ may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary Safety Evaluator assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 4. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is $\geq$ 70%).			
Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).		
Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg	
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.	
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? • Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? • *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as z and f), is there a different number or	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

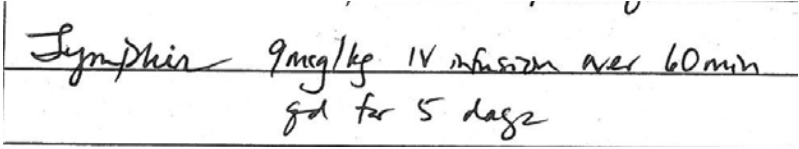
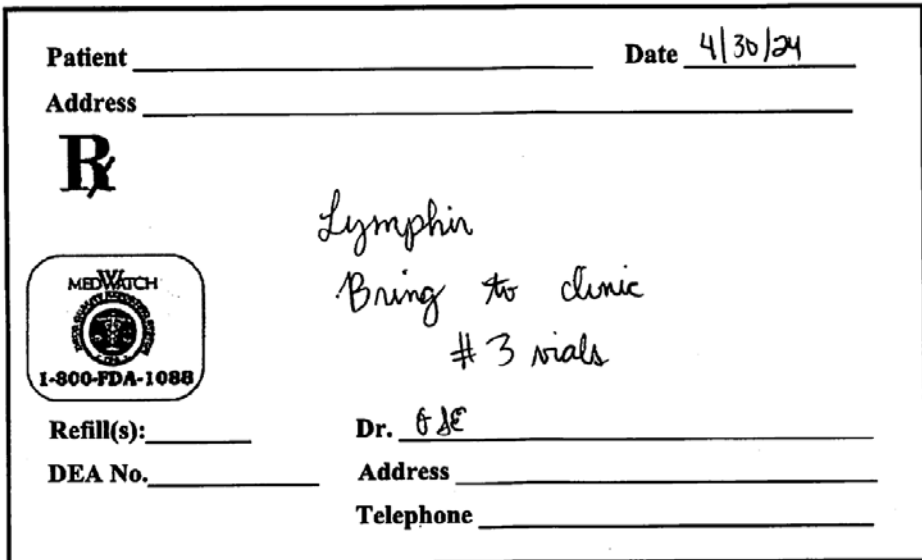
	placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	
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Table 6. Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

APPENDIX B. PRESCRIPTION SIMULATION SAMPLES AND RESULTS

Figure 1. Lymphir Study (Conducted on 4/30/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order: 	Lymphir Bring to clinic. Dispense 3 vials.
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Lymphir	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Lymphir					
People Received Study: 197					
People Responded: 87					
Total	24	24	17	22	87
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
JYMPHIR	2	0	0	0	2
LEMFEAR	0	0	1	0	1
LEMFERE	0	0	2	0	2
LIMFEAR	0	0	2	0	2
LIMFEER	0	0	1	0	1
LIMFER	0	0	1	0	1
LIMFERE	0	0	1	0	1
LIMPHERE	0	0	1	0	1
LIMVERE	0	0	1	0	1
LYMFEAR	0	0	3	0	3
LYMFEER	0	0	1	0	1
LYMFERE	0	0	1	0	1
LYMFIAR	0	0	1	0	1
LYMPHERE	0	0	1	0	1
LYMPHIA	0	1	0	0	1
LYMPHIN	0	15	0	0	15
LYMPHIR	10	8	0	22	40
SYMPHIR	7	0	0	0	7
TYMPHIR	4	0	0	0	4
TYMPHIS	1	0	0	0	1

APPENDIX E. MODERATELY SIMILAR NAMES (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Lymphir Pronunciation: lim' feer Established name: denileukin diftiox- cxdl Dosage form: for injection Strength(s): 300 mcg/vial Dosage: 9 mcg/kg/day administered as an intravenous infusion on days 1 through 5 of a 21-day treatment cycle	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	(b) (4) ***	63	Orthographically, the suffixes of the name pair (b) (4) provide sufficient orthographic differences. Specifically, the (b) (4) *** give the names different shapes when written. Phonetically, the second syllables (feer' vs. (b) (4) sound different. Although both Lymphir and (b) (4) ** are single strength products (300 mcg/vial vs. (b) (4)), where the strength may be omitted on a prescription order, this name pair differs based on route of administration (intravenous vs. (b) (4), recommended dosage (9 mcg/kg/day vs. (b) (4) and frequency (once daily on days 1 through 5 of a 21-day cycle vs. (b) (4). Additionally, Lymphir is an injectable oncology drug. Because injectable oncology drugs administered by healthcare professionals are not communicated by verbal order and

No.	Proposed name: Lymphir Pronunciation: lim' feer Established name: denileukin diftiox- cxdI Dosage form: for injection Strength(s): 300 mcg/vial Dosage: 9 mcg/kg/day administered as an intravenous infusion on days 1 through 5 of a 21-day treatment cycle	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
			typically undergo independent double checks by two pharmacists in the usual clinical setting, the likelihood of phonetic name confusion and the risk of both pharmacists overlooking the difference in route, dose, and frequency is minimized. Thus, the risk of name confusion between the name pair is minimized.

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/s/

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SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	4/18/2023
Responsible OND Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	IND 110489 BLA 761312
Product Name and Strength:	(denileukin diftitox-cxdl) for injection, 300 mcg per vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Citius Pharmaceuticals, Inc. (Citius)
FDA Received Date:	May 6, 2022 (IND) September 28, 2022 (BLA)
Nexus NPNS ID #:	2022-167 (IND) 2022-128 (BLA)
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD

1 PURPOSE OF REVIEW

This review summarizes our evaluation of the four-letter suffixes proposed by Citius for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761312.

1.1 Regulatory History

On October 14, 2022, under BLA 761312, Citius was notified of the Agency's intention to designate a nonproprietary name that includes a four-letter distinguishing suffix that is devoid of meaning for their product in an Advice Letter^a.

On March 31, 2023, via email communication, Citius inquired on the status of suffixes submitted under IND 110489 on May 6, 2022.^b

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On May 6, 2022, a list of 10 suffixes, in their order of preference, to be used in the nonproprietary name of their product was submitted to IND 110489^c. The May 6, 2022 submission also provided findings from an external study conducted by (b) (4), evaluating the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Citius:

^a Harris, D. General Advice Letter for BLA 761312. Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US) 2022 Oct 14.

^b On May 6, 2022, Eisai, Inc. submitted a list of 10 suffixes, in their order of preference, to be used in the nonproprietary name of their product, and findings from an external study conducted by (b) (4) to IND 110489. Of note, the sponsorship of IND 110489 has subsequently been transferred from Eisai Inc. to Citius Pharmaceuticals Inc. on March 2, 2023. Thus, Citius emailed on March 31, 2023 to inquire on the status of this May 6, 2022 submission. At the time of this review, DARRTS shows BLA 761312 makes reference to IND 110489.

^c Cover Letter – Request for Review of Nonproprietary Name Suffixes IND 110489. Nutley (NJ): Eisai, Inc.; 2022 May 06. Available from: <\\CDSESUB1\EVSPROD\ind110489\0101\m1\us\cover.pdf>

^d Data Summary for Proposed Suffixes IND 110489. (b) (4)
Available from: <\\CDSESUB1\EVSPROD\ind110489\0101\m1\us\1124-request-for-comments-advice-ind-suffixes.pdf>

Table 1. Suffixes submitted by Citius***			
1.	cxdl		
2.		(b) (4)	
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

We reviewed Citius’s proposed suffixes in the order of preference listed by Citius, along with the supporting data they submitted, using the principles described in the applicable guidance.^a

2.1 denileukin diftotox-cxdl

Citius’s first proposed suffix, -cxdl, is comprised of 4 distinct letters. We note that the letters ‘dl’ within the suffix represent the medical abbreviation for ‘deciliter’. We considered whether the inclusion of the letters ‘dl’ within the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

We determined that the proposed suffix -cxdl, is not too similar to any other products’ suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

^a Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

3 COMMUNICATION OF DMEPA 2 ANALYSIS

These findings were shared with OPDP. On April 12, 2023, OPDP did not identify any concerns that would render this proposed suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Hematologic Malignancies 2 (DHM 2) on April 18, 2023.

4 CONCLUSION

We find Citius's proposed suffix -cxdl acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to denileukin diftitox-cxdl. DMEPA 2 will communicate our findings to the Applicant via letter.

4.1 Recommendations for Citius Pharmaceuticals, Inc.

We find the nonproprietary name, denileukin diftitox-cxdl, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, denileukin diftitox-cxdl will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review.

However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we will inform you of our findings.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CARLOS M MENA-GRILLASCA
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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	March 23, 2022
Application Type and Number:	BLA 761312
Product Name and Strength:	Lymphir (denileukin diftitox-xxxx*) for Injection, 300 mcg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Citius Pharmaceuticals, Inc. (Citius)
PNR ID #:	2022-1044724914
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

* The nonproprietary name for Lymphir has not yet been determined; therefore, “denileukin diftitox-xxxx” is used throughout this review as the nonproprietary name for this product.

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Lymphir, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Citius submitted an external name study, conducted by (b) (4) for this proposed proprietary name.

1.1 REGULATORY HISTORY

We note that Ontak (denileukin diftitox) Injection was approved in 1999 under Eisai, Incorporated's application BLA 103767 for the treatment of adult patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor. On January 8, 2014, Eisai, Inc, notified the Agency that Ontak production was being discontinued due to manufacturing issues. BLA 103767 is still in active status at the time of this review.

For Citius's BLA 761312 that now seeks a similar indication as Ontak, BLA 761312 makes reference to Eisai Inc's BLA 103767 and IND 110489. Eisai Inc. previously submitted the proposed proprietary name, (b) (4) *** on February 24, 2022 under IND 110489. However, on June 23, 2022, we found the name, (b) (4) *** unacceptable due to phonetic similarities and overlapping product characteristics with the proprietary name, (b) (4) ** a

Eisai Inc. is an authorized US agent for Citius.

Citius submitted the name, Lymphir, for review on December 28, 2022. Per the 356h form for Citius's name submission, BLA 761312 is a 351(a) application.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on December 28, 2022.

- Intended Pronunciation: lim' feer
- Nonproprietary Name: denileukin diftitox-xxxx
- Indication of Use: For the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy, (b) (4)
- Route of Administration: Intravenous infusion
- Dosage Form: for Injection
- Strength: 300 mcg/vial
- Dose and Frequency: 9 mcg/kg/day administered as an intravenous infusion over 60 minutes on 5 consecutive days, followed by a rest period of 16 days.

^a Mena-Grillasca, C. Proprietary Name Review for (b) (4) (IND 110489). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 JUN 23. PNR ID No. 2022-1044724459.

- **How Supplied:** Supplied as a sterile, white, lyophilized powder for reconstitution in a single-dose vial containing 300 mcg denileukin diftitox-xxxx. Each carton contains one vial.
- **Storage:** Store in a refrigerator between 2°C to 8°C (36°F to 46°F). Do not freeze.

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Lymphir.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Lymphir would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Lymphir. The Division of Hematologic Malignancies 2 (DHM 2) concurred with the findings of OPDP's assessment for Lymphir.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Lymphir.

2.2.1 *United States Adopted Names (USAN) Search*

There is no USAN stem present in the proposed proprietary name^b.

2.2.2 *Components of the Proposed Proprietary Name*

Citius did not provide a derivation or intended meaning for the proposed proprietary name, Lymphir, in their submission. This proprietary name is comprised of a single word that contains the letter 'ir' in the suffix of the name, which is the abbreviation for 'immediate release'.

Although we typically discourage the inclusion of medical abbreviations in proprietary names, we note the letter strings 'IR' is a common letter strings in existing drug nomenclature (e.g., Advair, Humira, Levemir, etc.) and we are unaware of post-market reports of medication errors associated with these specific abbreviations through our routine surveillance. As the letter string 'IR' is located at the end of the name, we also evaluated the potential risk of misinterpreting the proposed proprietary name as "[drug name similar to Lymph] IR" and did not identify any names that would pose a risk for confusion.^c Furthermore, the letters 'ir' are not capitalized, or bolded, to make the letters 'ir' more prominent in the name. Therefore, in this case we do not object to the proposed proprietary name based on the inclusion of this medical abbreviation.

Lymphir does not contain any other components (i.e., a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

^b USAN stem search conducted on March 1, 2023.

^c POCA search for 'Lymph' conducted on March 2, 2023.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, February 6, 2023 email, the Division of Hematologic Malignancies 2 (DHM 2) expressed concerns about a “look-alike and sound-alike” potential with the proposed proprietary name, Lymphir and the currently marketed product, Levemir (BLA 021536). However, DHM2 noted differences in the treatment setting [oncology vs endocrinology (diabetes)] and route of administration (intravenous vs. subcutaneous). In addition, since Lymphir will be administered in a healthcare facility, they did not have major concerns that the two products would lead to medication errors.

We evaluated this name pair and determined that the risk of confusion will be mitigated because there are sufficient orthographic and phonetic differences.

Orthographically, Lymphir has the downstroke letters ‘y’ and ‘p’ in the second and fourth positions, respectively which is absent from Levemir.

Phonetically, Lymphir is comprised of two syllables whereas Levemir is comprised of three syllables. The ending of the first syllables (‘Lim-’ vs. ‘Le’) and second syllables (‘-feer’ vs. ‘-ve-’) sound different.

These differences are further supported by FDA’s Phonetic and Orthographic Computer Analysis (POCA) program^d, which calculates a combined orthographic and phonetic score of 53%, suggesting that there is low similarity between these names (see Appendix F).

2.2.4 FDA Name Simulation Studies

Ninety-five (n = 95) practitioners participated in DMEPA’s prescription studies for Lymphir. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^e identified 17 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score $\geq 70\%$. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and DHM2. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names

^d POCA search conducted on March 17, 2023 in version 5.2.

^e POCA search conducted on January 27, 2023 in version 5.2.

Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	15
Low similarity name pair: combined match percentage score $\leq 54\%$	2

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 18 names contained in Table 1 determined none of the names will pose a risk for confusion with Lymphir as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On March 22, 2023, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 2 (DHM 2).

3 CONCLUSION

The proposed proprietary name, Lymphir, is conditionally acceptable.

If you have any questions or need clarifications, please contact Wana Manitsitkul, OSE project manager, at 240-402-4156.

3.1 COMMENTS TO CITIUS PHARMACEUTICALS, INC.

We have completed our review of the proposed proprietary name, Lymphir, and have concluded that this name is conditionally acceptable.

If any of the proposed product characteristics as stated in your submission, received on December 28, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. **USAN Stems** (<https://www.ama-assn.org/about/united-states-adopted-names-approved-stems>)

USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm

(<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html>).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. 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.^f

^f National Coordinating Council for Medication Error Reporting and Prevention. <https://www.nccmerp.org/about-medication-errors> Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	Is the proposed name obviously similar in spelling and pronunciation to other names?
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	Are there inert or inactive ingredients referenced in the proprietary name?
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	Does the proprietary name include combinations of active ingredients?
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	Is there a United States Adopted Name (USAN) stem in the proprietary name?
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	Is this proprietary name used for another product that does not share at least one common active ingredient?
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	Is this a proprietary name of a discontinued product?
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, Cerner RxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.

- Low similarity: combined match percentage score $\leq 54\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names⁸. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
 - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

⁸ Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

Four 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, verbal pronunciation of the drug name or during computerized provider order entry. 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 vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

- d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is $\geq 70\%$).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.

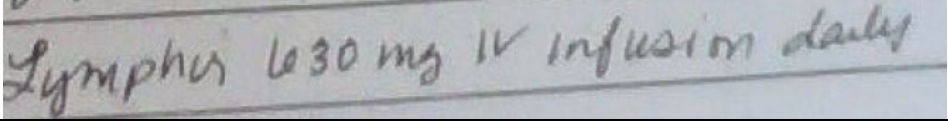
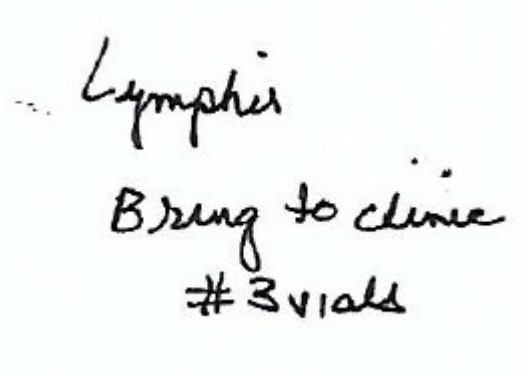
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Lymphir Study (Conducted on January 20, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Lymphir Bring to clinic #3 vials
<u>Outpatient Prescription:</u> 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Lymphir	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Lymphir

As of Date 3/2/2023

258 People Received

Study

95 People Responded

Study Name: Lymphir

Total	25	27	22	21	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
LEMVIR	0	0	3	0	3
LIMFERE	0	0	4	0	4
LIMFIR	0	0	2	0	2
LIMVEER	0	0	3	0	3
LIMVER	0	0	1	0	1
LIMVIR	0	0	3	0	3
LINFEAR	0	0	1	0	1
LUMPHIR	1	0	0	0	1
LYMFEAR	0	0	1	0	1
LYMFIR	0	0	1	0	1
LYMPHA	1	0	0	0	1
LYMPHEER	0	0	1	0	1
LYMPHEI	0	0	0	1	1
LYMPHER	5	0	0	0	5
LYMPHI	0	0	0	1	1
LYMPHIA	0	0	0	1	1
LYMPHIR	16	27	0	13	56
LYMPHIS	1	0	0	4	5
LYMPHOR	1	0	0	0	1
LYMPHRERE	0	0	1	0	1
LYMPHRI	0	0	0	1	1
LYMVIR	0	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is $\geq 70\%$)

No.	Proposed name: Lymphir Established name: denileukin diftitox-xxxx Dosage form: for Injection Strength(s): 300 mcg/vial Usual Dose: 9 mcg/kg/day administered as an intravenous infusion on 5 consecutive days.	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Lymphir***	100	Subject of this review.

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Camphor	56
2.	Camphor, (-)-	56

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Lymphir Established name: denileukin diftitox-xxxx Dosage form: for Injection Strength(s): 300 mcg/vial Usual Dose: 9 mcg/kg/day administered as an intravenous infusion on 5 consecutive days.	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	Lampit	62	This name pair has sufficient orthographic and phonetic differences.
2.	Lipitor	58	This name pair has sufficient orthographic and phonetic differences
3.	Lamisil	56	This name pair has sufficient orthographic and phonetic differences.
4.	(b) (4) ***	56	Orthographically, the suffixes ('-phir' vs. (b) (4)) of the name pair provide some orthographic differences. Phonetically, the ending of the ending of the second syllables ('-feer' vs. '-(b) (4)' sound different. Although Lymphir and (b) (4) *** are both single strength products (300 mcg/vial vs. (b) (4)), where

No.	Proposed name: Lymphir Established name: denileukin diftitox-xxxx Dosage form: for Injection Strength(s): 300 mcg/vial Usual Dose: 9 mcg/kg/day administered as an intravenous infusion on 5 consecutive days.	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
			the strength may be omitted on a prescription order, this name pair differs in route of administration (intravenous infusion vs. (b) (4) and frequency of administration (daily on 5 consecutive days vs. (b) (4)). Thus, the risk of name confusion between the name pair is minimized.
5.	Lumify	55	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
1.	Levemir	53
2.	Demser	52

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Lypsyl	62	International product formerly marketed in Canada.
2.	Lymphazurin	58	Brand discontinued with no generic equivalents available. NDA 018310 withdrawn FR effective 01/05/2015.
3.	Lidovir	56	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
4.	(b) (4) ***	56	Proposed proprietary name for NDA 213716 found unacceptable by DMEPA (2020-38457926; June 8, 2020). Product approved under proprietary name Lupkynis on 1/22/2021.
5.	(b) (4) ***	56	Proposed proprietary name for BB-IND 16675.231 found unacceptable by CBER. BLA 125703 was approved under the proprietary name, Tecartus.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^h.

No.	Name	POCA Score (%)
1.	Men-Phor	58
2.	Famvir	56
3.	Msir	56

^h Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

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