

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

213972Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	July 15, 2024
Application Type and Number:	NDA 213972
Product Name, Dosage Form, and Strength:	Orlynvah (sulopenem etzadroxil and probenecid) Tablets, 500 mg/500 mg
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Iterum Therapeutics US Limited (Iterum)
PNR ID #:	2024-1044725749
DMEPA 1 Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD
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1 INTRODUCTION

This review evaluates the proposed proprietary name, Orlynvah, 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. Iterum submitted an external name study, conducted by (b) (4), for this proposed proprietary name. Additionally, we note that Iterum previously submitted a different external name study, also conducted by (b) (4), that was previously reviewed under NDA 213972 (see Section 1.1 below).

1.1 REGULATORY HISTORY

Iterum previously submitted the proposed proprietary name, (b) (4)*** on March 13, 2020. However, we found the name, (b) (4)*** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, Orvaten, as well as similarity in pronunciation with the proposed proprietary name, (b) (4)***, under IND 129849 on August 26, 2020.^c

Subsequently, Iterum submitted the proposed proprietary name, Orlynvah***, under NDA 213972 on January 13, 2021, and we found the name conditionally acceptable on April 5, 2021.^d

On July 23, 2021, NDA 213972 received a Complete Response Letter (CRL).^e

On April 25, 2024, Iterum resubmitted NDA 213972, which included responses to the deficiencies included in the Agency's CRL dated July 23, 2021.^f

Subsequently, Iterum submitted the proposed proprietary name, Orlynvah, for review on April 26, 2024 under NDA 213972.^g

^a Proprietary Name Safety Summary for Orlynvah. Miami (FL): (b) (4) 2023 DEC 26. Available from: [\\CDSESUB1\EVSPROD\nda213972\0072\m1\us\proprietary-name-safety-summary-for-orlynvah-\(b\)\(4\)-26-dec-202.pdf](\\CDSESUB1\EVSPROD\nda213972\0072\m1\us\proprietary-name-safety-summary-for-orlynvah-(b)(4)-26-dec-202.pdf).

^b Orlynvah Proprietary Name Safety Summary. Miami (FL): (b) (4) 2020 NOV 20. Available from: [\\CDSESUB1\EVSPROD\nda213972\0005\m1\us\orlynvah-proprietary-name-safety-summary-by-\(b\)\(4\).pdf](\\CDSESUB1\EVSPROD\nda213972\0005\m1\us\orlynvah-proprietary-name-safety-summary-by-(b)(4).pdf).

^c Farshneshani, Z. Proprietary Name Review for (b) (4)*** (IND 129849). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 AUG 26. Panorama No. 2020-38467346.

^d Myers, D. Proprietary Name Review for Orlynvah*** (NDA 213972). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 APR 05. PNR ID No. 2021-1044697153.

^e Smith, C. Communication: Complete Response Letter for sulopenem etzadroxil and probenecid tablets. Silver Spring (MD): FDA, CDER, OND, OAP, DAI (US); 2021 JUL 23. NDA 213972. Available from: <https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af80604baa>.

^f Cover Letter: Resubmission of NDA 213972 for Orlynvah (NDA 213972). Old Saybrook (CT): Iterum Therapeutics US Limited; 2024 APR 25. Available at: <\\CDSESUB1\EVSPROD\nda213972\0070\m1\us\cover-letter.pdf>.

^g Cover Letter: Request for Proprietary Name Review for Orlynvah (NDA 213972). Chicago (IL): Iterum Therapeutics US Limited; 2024 APR 26. Available at: <\\CDSESUB1\EVSPROD\nda213972\0072\m1\us\cover-letter.pdf>.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on April 26, 2024^h, and the prescribing information received on April 25, 2024.ⁱ

Table 1. Relevant Product Information for Orlynvah	
Intended pronunciation:	or lin' vah
Active ingredient:	sulopenem etzadroxil and probenecid
Indication:	In adult women $\geq$ 18 years of age for the treatment of uncomplicated urinary tract infections caused by designated susceptible microorganisms.
Dosage Form:	Tablets
Strength:	500 mg/500 mg
Route of administration:	Oral
Dose and frequency:	one tablet twice daily for 5 days
How Supplied:	Bottles of 10 tablets with child-resistant caps Bottles of 30 tablets with child-resistant caps
Storage:	Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room temperature].
Listed Drug (for the active ingredient probenecid):	Benemid (probenecid) NDA 007898

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Orlynvah would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Orlynvah. The Division of Anti-Infectives (DAI) concurred with the findings of OPDP's assessment for Orlynvah.

^h Table of Proprietary Name Information for Orlynvah (NDA 213972). Chicago (IL): Iterum Therapeutics US Limited; 2024 APR 26. Available from: <\\CDSESUB1\EVSPROD\nda213972\0072\m1\us\table-of-proprietary-name-information-for-orlynvah.pdf>.

ⁱ Proposed prescribing information for Orlynvah. Old Saybrook (CT): Iterum Therapeutics US Limited; 2024 APR 25. Available from: <\\CDSESUB1\EVSPROD\nda213972\0070\m1\us\sulopenem-etzadroxil-draft-uspi-draft-17apr2024final.pdf>.

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Iterum did not provide a derivation or intended meaning for the proposed proprietary name, Orlynvah, in their submission. This proprietary name is comprised of a single word that includes the letter string, '-va-', a medical abbreviation for "visual acuity." In some circumstances, the incorporation of medical abbreviations in proprietary names can inadvertently be a source of error. For more information see draft guidance, *Best Practices in Developing Proprietary Names for Human Prescription Drug Products*.^k Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the abbreviation, 'va', in the infix of the name is unlikely to be separated from the surrounding letters in a manner that would lead to confusion. Thus, in this case, we do not object to the inclusion of the letter string 'va' in the infix of the proposed proprietary name.

Beyond this aforementioned abbreviation, we note that Orlynvah does not contain any 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 May 30, 2024, the Division of Anti-Infectives (DAI) did not forward any comments or concerns relating to Orlynvah at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Ninety-two (92) practitioners participated in DMEPA's prescription simulation studies for Orlynvah.

One respondent in the Computerized Prescription Order Entry (CPOE) study incorrectly selected the name "Vegzelma." However, the participant entered an incorrect sequence of letters, 'veg' when searching for the study name. As a result, the CPOE generated picklist did not contain Orlynvah as a choice. The participant proceeded to incorrectly select "Vegzelma" as their response after 40 seconds in order to proceed with the FDA prescription stimulation study. Thus, in this case, the study response is unlikely to be representative of a plausible CPOE based risk. Despite this, we further evaluated Orlynvah *versus* Vegzelma and determined that this name pair has sufficient orthographic and phonetic differences.

^j USAN stem search conducted on May 2, 2024.

^k Guidance for Industry: Best Practices in Developing Proprietary Names for Human Prescription Drug Products. 2020. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

Orthographically, the first letters are different ('O' *versus* 'V'). Additionally, the upstrokes of the letter 'l' in the third position and the letter 'h' in the eighth position of Orlynvah and the upstroke letter 'l' in the sixth position of Vegzelma, provide sufficient orthographic differences. Phonetically, the first syllables (or *versus* veg) and second syllables (lin *versus* zel) sound different and provide sufficient phonetic differences.

Additionally, the product characteristics between the name pair are different. Specifically, Orlynvah does not overlap with Vegzelma in dose (one tablet (500 mg/500 mg) *versus* 5 mg/kg, 10 mg/kg, or 15 mg/kg) or frequency (twice daily for 5 days *versus* every 2 week or every 3 weeks). Furthermore, there is no overlap in route of administration (oral *versus* intravenous infusion), or dosage form (tablet *versus* injection), if included on the prescription/medication order.

Furthermore, we note that Vegzelma is an injectable oncology product, indicated for the treatment of metastatic colorectal cancer, first-line non-squamous non-small cell lung cancer, recurrent glioblastoma, metastatic renal cell carcinoma, persistent, recurrent, or metastatic cervical cancer, and epithelial ovarian, fallopian tube, or primary peritoneal cancer, and that injectable oncology drugs typically undergo independent double checks by two pharmacists in the usual clinical setting. Therefore, the likelihood of both pharmacists overlooking the difference in dose and frequency of administration is minimized.

When all the aforementioned mitigations are considered in totality, we find the risk of name confusion is adequately minimized in this case (see Appendix E).

Additionally, one respondent in the verbal study misinterpreted the proposed name as "Olinva", which is a close hit to the currently marketed product Olinvyk. We further evaluated the name pair, Orlynvah *versus* Olinvyk and determined there is sufficient orthographic, phonetic, and product characteristic differences between the name pair.

Orthographically, the downstroke of the letter 'y' in the fourth position of Orlynvah *versus* dotted letter 'i' in the third position and downstroke of the letter 'y' in the seventh position of Olinvyk, provides some orthographic differences.

Phonetically, the third syllables (vah *versus* vick) provide some phonetic difference.

Additionally, the product characteristics between the name pair are different. Specifically, Orlynvah does not overlap with Olinvyk in strength (500 mg/500 mg *versus* 1 mg/mL, 2 mg/2 mL, and 30 mg/30 mL (1 mg/1 mL), in dose (one (500 mg/500 mg) tablet *versus* initiate treatment with a 1.5 mg dose, for patient controlled analgesia (PCA), recommended demand dose is 0.35 mg, with a 6-minute lock-out or supplemental doses of 0.75 mg can be administered, beginning 1 hour after the initial dose, and hourly thereafter, as needed), or frequency (twice a day *versus* for PCA a 6-minute lock-out or supplemental doses can be administered, beginning 1 hour after the initial dose, and hourly thereafter). Furthermore, there is no overlap in route of administration (oral *versus* intravenous), or dosage form (tablet *versus* injection), if included on the prescription/medication order.

When all the aforementioned mitigations are considered in totality, we find the risk of name confusion is adequately minimized in this case (see Appendix E).

The remaining 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 search¹ identified 19 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 4 names not previously analyzed. These names are 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, FDA Prescription Simulation Study, and (b) (4) external study. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	3
Low similarity name pair: combined match percentage score $\leq 54\%$	4

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

Our analysis of the 8 names contained in Table 2 determined none of the names will pose a risk for confusion with Orlynvah as described in Appendices C through H.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On July 15, 2024, DMEPA 1 communicated our determination to the Division of Anti-Infectives (DAI).

3 CONCLUSION

The proposed proprietary name, Orlynvah, is conditionally acceptable.

¹ POCA search conducted on May 2, 2024 in version 5.8.

If you have any questions or need clarifications, please contact Amy Chung, OSE project manager, at (240) 402-4547.

3.1 COMMENTS TO ITERUM THERAPEUTICS US LIMITED

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

If any of the proposed product characteristics as stated in your submission, received on April 26, 2024, are 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.^m

*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.

^m 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.
 - 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 namesⁿ. 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 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.

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

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 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?		

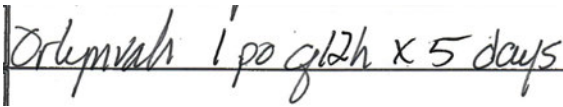
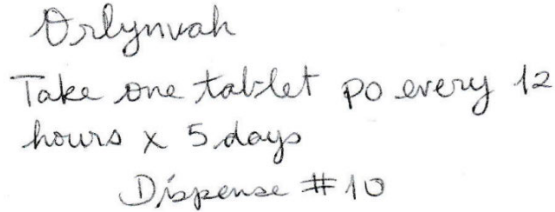
Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).			
Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths 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.		
	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; vertical-align: top;"> 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 </td> <td style="width: 50%; vertical-align: top;"> 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? </td> </tr> </table>	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	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?
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	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 $\leq 69\%$).		
	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?	

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. Orlynvah Study (Conducted on 5/3/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order: 	Orlynvah Take one tablet by mouth every 12 hours for 5 days Dispense 10
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Orlynvah	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Orlynvah					
People Received Study: 197					
People Responded: 92					
Total	26	20	19	27	92
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
FORLIMBA	0	0	1	0	1
FORLYNVA	0	0	1	0	1
OLINVA	0	0	1	0	1
ORHPRVAH	1	0	0	0	1
ORLEMVAH	1	0	0	0	1
ORLENVA	0	0	1	0	1
ORLEPVAH	1	0	0	0	1
ORLIMVA	0	0	1	0	1
ORLIMVAB	1	0	0	0	1
ORLIMVAH	3	0	0	0	3
ORLINVA	0	0	10	0	10
ORLIPIVAH	1	0	0	0	1
ORLYMVAH	8	0	0	0	8
ORLYMVALS	1	0	0	0	1

ORLYNBA (?)	0	0	1	0	1
ORLYNVA	0	0	2	0	2
ORLYNVAH	9	19	0	26	54
ORLYNVAK	0	1	0	0	1
PROLINVA	0	0	1	0	1
VEGZELMA	0	0	0	1	1

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is $\geq 70\%$)

No.	Proposed name: Orlynvah Pronunciation: or lin' vah Established name: sulopenem etzadroxil and probenecid Dosage form: Tablets Strength(s): 500 mg/500 mg Dosage: one tablet twice daily for 5 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.	Orlynvah	100	This name is the 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.	N/A	

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: Orlynvah Pronunciation: or lin' vah Established name: sulopenem etzadroxil and probenecid Dosage form: Tablets Strength(s): 500 mg/500 mg Dosage: one tablet twice daily for 5 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.	Olinvyk	59	See FMEA in Section 2.2.4.
2.	(b) (4) ***	52	This name pair has sufficient orthographic and phonetic differences.
3.	Vegzelma	24	See FMEA in Section 2.2.4.

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
1.	Orlistat	54
2.	Oralone	51

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.	(b) (4) ***	64	Name entered by Safety Evaluator. The proposed proprietary name, (b) (4) ***, has not been submitted to the Agency for review.
2.	(b) (4) ***	57	Proposed proprietary name for (b) (4) found unacceptable, due to a conflict with a marketed product, by DMEPA (PNR ID # (b) (4)). Subsequently, the Applicant submitted a Request for Reconsideration of the proposed proprietary name, which was again found unacceptable, due to a conflict with a marketed product, by DMEPA (b) (4).

APPENDIX H. Names not likely to be confused due to absence of attributes that are known to cause name confusion^o.

No.	Name	POCA Score (%)
1.	N/A	

^o 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

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/

DEBORAH E MYERS
07/16/2024 09:36:32 AM

VALERIE S VAUGHAN
07/16/2024 09:43:22 AM

IDALIA E RYCHLIK
07/16/2024 10:54:36 AM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
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:	April 5, 2021
Application Type and Number:	NDA 213972
Product Name and Strength:	Orlynvah (sulopenem etzadroxil and probenecid) Tablets, 500 mg/500 mg
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Iterum Therapeutics, Inc. (Iterum)
PNR ID#:	2021-1044697153
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Team Leader (Acting):	Valerie Vaughan, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Orlynvah, 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. Iterum submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

1.1 REGULATORY HISTORY

Iterum previously submitted the proposed proprietary name, (b) (4)*** on March 13, 2020. However, we found the name, (b) (4)*** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, Orvaten, as well as similarity in pronunciation with the proposed proprietary name, (b) (4)***, under IND 129849 on August 26, 2020.^a

Thus, Iterum submitted the name, Orlynvah, for review on January 13, 2021.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on January 13, 2021.

- Intended Pronunciation: or lin' vah
- Active Ingredient: sulopenem etzadroxil and probenecid
- Indication of Use: in adult women $\geq$ 18 years of age for the treatment of uncomplicated urinary tract infections caused by designated susceptible microorganisms proven or strongly suspected to be nonsusceptible to a quinolone: *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*.
- Route of Administration: Oral
- Dosage Form: Tablets
- Strength: 500 mg/500 mg
- Dose and Frequency: one tablet twice daily for 5 days
- How Supplied: Bottles of 30 tablets with child-resistant caps, bottles of 10 tablets with child-resistant caps (b) (4)
- Storage: Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room temperature].

2 RESULTS

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

^a Farshneshani, Z. Proprietary Name Review for (b) (4)*** (IND 129849). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 AUG 26. Panorama No. 2020-38467346.

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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

Iterum did not provide a derivation or intended meaning for the proposed proprietary name, Orlynvah, in their submission. This proprietary name is comprised of a single word. We note that Orlynvah includes the letter strings; 'Or-', a medical abbreviation for "operating room", '-nv-', a medical abbreviation for "nausea and vomiting", '-va-', a medical abbreviation for "visual acuity", and '-ah' a medical abbreviation for "hypermetropic astigmatism." In some circumstances, the incorporation of medical abbreviations in proprietary names can inadvertently be a source of error. For more information see the Guidance for Industry, "Best Practices in Developing Proprietary Names for Human Prescription Drug Products."^c

Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the abbreviations, 'Or-' in the prefix, '-nv-' and '-va' in the infix, and '-ah' in the suffix of the name, are unlikely to be separated from the surrounding letters in a manner that would lead to confusion in this case. Thus, in this case, we do not object to the inclusion of these abbreviations.

Beyond these abbreviations we note that Orlynvah does not contain any additional components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 22, 2021 e-mail, the Division of Anti-Infectives (DAI) did not forward any comments or concerns relating to Orlynvah at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-six practitioners participated in DMEPA's prescription studies for Orlynvah.

^b USAN stem search conducted on January 14, 2021.

^c This guidance represents FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

In the computerized provider order entry (CPOE) simulation study, one participant entered an incorrect sequence of letters, “ong” instead of “orl,” when searching for the study name, which generated a pick list that did not contain the proposed study name “Orlynvah.” After 18 seconds passed, the participant then incorrectly selected “Onglyza,” suggesting that the participant selected a random name in order to proceed with the simulation study. Thus, in this case, the study response is unlikely to be representative of a plausible CPOE based risk. Despite this, we further evaluated the name pair “Orlynvah” and “Onglyza” in Appendix E and determined that these names have sufficient orthographic and phonetic differences. Therefore, we find that this name pair could safely coexist on the market due to low risk for name confusion. Furthermore, we note this name pair has a combined phonetic and orthographic computer analysis (POCA) score of 48 indicating that there is low similarity between this name pair, which further supports our conclusion that this name pair could safely coexist on the market.

Additionally, one participant in the voice simulation study commented that the proposed proprietary name, “Orlynvah” is “too similar to Orilissa.” We further evaluated the name pair “Orlynvah” and “Orilissa” in Appendix E and determined that these names have sufficient orthographic and phonetic differences. Therefore, we find that this name pair could safely coexist on the market due to low risk for name confusion. Furthermore, we note this name pair has a combined POCA score of 46 indicating that there is low similarity between this name pair, which further supports our conclusion that this name pair could safely coexist on the market.

The remaining 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^d identified 15 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 FDA Prescription Simulation Study. 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
Highly similar name pair: combined match percentage score $\geq 70\%$	0

^d POCA search conducted on January 14, 2021 in version 4.4.

Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	13
Low similarity name pair: combined match percentage score $\leq 54\%$	4

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

Our analysis of the 17 names contained in Table 1 determined none of the names will pose a risk for confusion with Orlynvah as described in Appendices C through H.

2.2.8 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anti-Infectives (DAI). At that time we also requested additional information or concerns that could inform our review. On April 3, 2021, the Division of Anti-Infectives (DAI) stated no additional concerns with the proposed proprietary name, Orlynvah.

3 CONCLUSION

The proposed proprietary name, Orlynvah, is acceptable.

If you have any questions or need clarifications, please contact Nicholas Miles, OSE project manager, at 301-796-7025.

3.1 COMMENTS TO ITERUM THERAPEUTICS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on January 13, 2021, 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. ^e

^e 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, CernerRxNorm, 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 names^f. 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

^f 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. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed 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 <i>z</i> and <i>f</i>), 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 with overlapping or similar strengths or doses.

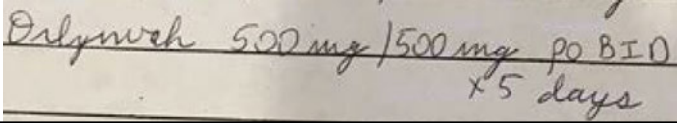
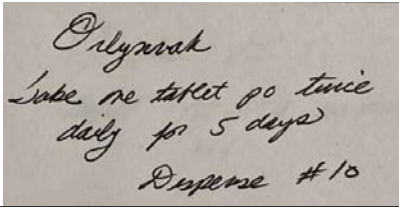
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), 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 as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤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. Orlynvah Study (Conducted on January 22, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Orlynvah Take one tablet by mouth twice daily for 5 days
Outpatient Prescription: 	Dispense #10
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Orlynvah	

FDA Prescription Simulation Responses (Aggregate Report)

209 People Received Study
86 People Responded

Study Name: Orlynvah

Total	17	30	21	18	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
ONGLYZA	0	1	0	0	1
ORLEZA	0	0	1	0	1
ORLIMVA	0	0	1	0	1
ORLINBA	0	0	2	0	2
ORLINVA	0	0	12	0	12
ORLINZA	0	0	5	0	5
ORLYNUAH	0	0	0	1	1
ORLYNVAH	0	29	0	14	43
ORLYNVAK	16	0	0	0	16
ORLYORAK	1	0	0	0	1
ORLYUVAK	0	0	0	1	1
ORLYUVAL	0	0	0	1	1
ORLYWAH	0	0	0	1	1

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

No.	Proposed name: Orlynvah Established name: sulopenem et zadroxil and probenecid Dosage form: Tablets Strength(s): 500 mg/500 mg Usual Dose: one tablet twice daily for 5 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.	N/A		

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.	Olinvyk	59

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: Orlynvah Established name: sulopenem et zadroxil and probenecid Dosage form: Tablets Strength(s): 500 mg/500 mg Usual Dose: one tablet twice daily for 5 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.	Norliqva***	64	This name pair has sufficient orthographic and phonetic differences.
2.	Loryna	56	This name pair has sufficient orthographic and phonetic differences.
3.	(b) (4)***	55	(b) (4)

No.	Proposed name: Orlynvah Established name: sulopenem etzadroxil and probenecid Dosage form: Tablets Strength(s): 500 mg/500 mg Usual Dose: one tablet twice daily for 5 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
			(b) (4)
4.	Onglyza	48	This name pair has sufficient orthographic and phonetic differences.
5.	Orilissa	48	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.	Lynoral	48
2.	Norval	44

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.	Orlenta	66	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
2.	(b) (4) ***	60	Proposed proprietary name for (b) (4) found unacceptable by DMEPA (b) (4). Subsequently, the proposed proprietary name (b) (4) *** was found conditionally acceptable for (b) (4).
3.	(b) (4) ***	58	Proposed proprietary name for IND 109886 was withdrawn by the Applicant on December 12, 2018. Product approved on February 27, 2020, with the proprietary name, Nurtec ODT under NDA 212728.
4.	(b) (4) ***	56	Proposed proprietary name for (b) (4) was withdrawn by the Applicant on (b) (4). Subsequently, (b) (4) was withdrawn on (b) (4).
5.	Orlex HC	56	Brand discontinued with no generic equivalents available. ANDA 086844 withdrawn FR effective 06/19/1995.

No.	Name	POCA Score (%)	Failure preventions
6.	(b) (4)***	56	Proposed proprietary name for IND 104676 was withdrawn by the Sponsor on October 11, 2017. Subsequently, the product was approved on February 14, 2018, with the proprietary name Erleada under NDA 210951.

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

No.	Name	POCA Score (%)
1.	Tri-Linyah	59
2.	(b) (4)***	56
3.	Relenza	56

^g 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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