

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

210730Orig1s000

PROPRIETARY NAME REVIEW(S)

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:	May 1, 2020
Application Type and Number:	NDA 210730
Product Name and Strength:	Olinvyk (oliceridine) injection, 1 mg/ml
Total Product Strength:	1 mg/ml, 2 mg/ml, 30mg/30ml
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Trevana, Inc (Trevana)
Panorama #:	2020-37752613
DMEPA Safety Evaluator:	Zahra Farshneshani, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD

Contents

1	INTRODUCTION	1
1.1	Regulatory History	1
1.2	Product Information	1
2	RESULTS.....	1
2.1	Misbranding Assessment	1
2.2	Safety Assessment.....	2
3	CONCLUSION	4
3.1	Comments to the Applicant/Sponsor	4
4	REFERENCES	4
	APPENDICES	5

1 INTRODUCTION

This review evaluates the proposed proprietary name, Olinvyk, 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. Trevana submitted an external name study; however, the company that performed the external name study was not identified in the proprietary name submission.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Olinvo***, on March 4, 2016 which was found to be conditionally acceptable.^a The Applicant resubmitted the name, Olinvo***, on December 11, 2017 under NDA 210730. However, we found the name, Olinvo***, unacceptable (b) (4)

The Applicant then submitted the name, Olinvyk, for review on June 26, 2018 in which we found acceptable on August 6, 2018.^c However, a Complete Response letter was issued to Trevana on November 2, 2018 due to clinical deficiencies.

On February 7, 2020, Trevana submitted their Complete Response to the clinical deficiencies and indicated their request for proprietary name review would be submitted at a later date. Subsequently, Trevana submitted the name, Olinvyk, for review on February 10, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 7, 2020 and February 10, 2020.

- Intended Pronunciation: oh-LIN-vick
- Active Ingredient: oliceridine
- Indication of Use: management of moderate to severe acute pain in adults for whom an IV opioid is warranted
- Route of Administration: intravenous
- Dosage Form: injection
- Strength: 1 mg/ml, 2 mg/ml, 30mg/30ml; (1 mg/ml)
- Dose and Frequency:

^a Shah, M. Proprietary Name Review for Olinvo*** (IND 113537). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 25. Panorama No. 2016-2986617.

^b Johnson, C. Proprietary Name Review for Olinvo*** (NDA 210730). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 MAR 9. Panorama No. 2017-19602967.

^c Johnson, C. Proprietary Name Review for Olinvyk (NDA 210730). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 AUG 6. Panorama No. 2018-24104240.

Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed

Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed

- How Supplied: 1mg/mL in 2 mL glass vial, 2mg/2mL in 2 mL glass vial, 30 mg/30 mL in 30 mL glass vial
- Storage: Room temperature

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Olinvyk would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) concurred with the findings of OPDP's assessment for Olinvyk.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Trevana did not provide a derivation or intended meaning for the proposed proprietary name, Olinvyk, in their submission. This proprietary name is comprised of a single word that does not contain any 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, March 16, 2020 e-mail, the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) did not forward any comments or concerns relating to Olinvyk at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

93 practitioners participated in DMEPA's prescription studies for Olinvyk. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to

^d USAN stem search conducted on April 20, 2020.

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 the combined score of $\geq 55\%$ or 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 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, FDA Prescription Simulation Study, other disciplines, and an undisclosed external 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
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 name contained in Table 1 determined that the name will not pose a risk for confusion with Olinvyk as described in Appendix D.

2.2.8 *Communication of DMEPA's Analysis at Midpoint of Review*

DMEPA communicated our findings to the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) via e-mail on April 28, 2020. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) on May 1, 2020, they stated no additional concerns with the proposed proprietary name, Olinvyk.

^e POCA search conducted on April 20, 2020 in version 4.3.

3 CONCLUSION

The proposed proprietary name, Olinvyk, is acceptable.

If you have any questions or need clarifications, please contact Ruth Madero, OSE project manager, at (240)402-4232.

3.1 COMMENTS TO TREVANA, INC

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

If any of the proposed product characteristics as stated in your submission, received on February 10, 2020, 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.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

***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^g. 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

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

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 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 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.

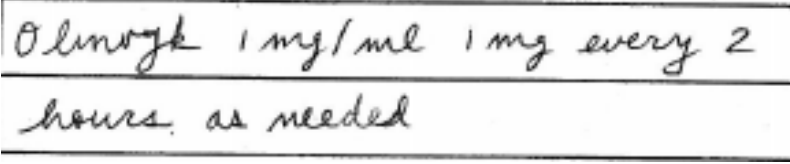
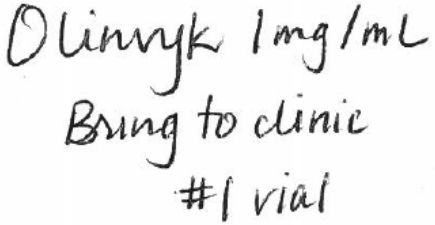
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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?
--	--	---

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. Olinvyk Study (Conducted on February 25, 2020)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Olinvyk 1 mg/mL. Bring to clinic. Dispense one vial.
<u>Outpatient Prescription:</u> 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Olinvyk	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Olinvyk

As of Date 4/24/2020

210 People Received Study
93 People Responded

Study Name: Olinvyk

Total	21	17	35	20	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
ALEMBIC	0	0	1	0	1
ALYMBIC	0	0	1	0	1
OLEMBIC	0	0	2	0	2
OLENZIC	0	0	1	0	1
OLENZIK	0	0	1	0	1
OLIMBIC	0	0	3	0	3
OLIMBICK	0	0	2	0	2
OLIMBIQ	0	0	2	0	2
OLINOVYK	0	0	0	1	1
OLINOYK	0	0	0	2	2
OLINUYSK	0	0	0	1	1
OLINVIC	0	0	5	0	5
OLINVIK	0	0	2	0	2
OLINVKYK	20	17	0	14	51
OLINYK	1	0	0	0	1
OLINZIC	0	0	2	0	2
OLUNVKYK	0	0	0	1	1

OLYMBIC	0	0	8	0	8
OLYMBIC 1 MG/LITER	0	0	1	0	1
OLYNVIC	0	0	2	0	2
OLYNVYK	0	0	0	1	1
OLYNZIC	0	0	1	0	1
ONLINVIC	0	0	1	0	1

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

No.	Proposed name: Olinvyk Established name: oliceridine Dosage form: injection Strength(s): 1 mg/ml Usual Dose: Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed	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.
	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.	(b) (4)	61

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: Olinvyk Established name: oliceridine Dosage form: injection Strength(s): 1 mg/ml Usual Dose: Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed	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
	N/A		

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

No.	Name	POCA Score (%)
	N/A	

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
	N/A		

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 (%)
	N/A	

^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

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/

ZAHRA FARSHNESHANI
05/04/2020 10:01:03 AM

OTTO L TOWNSEND
05/04/2020 12:54:58 PM

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:	August 6, 2018
Application Type and Number:	NDA 210730
Product Name and Strength:	Olinvyk (oliceridine) injection, 1 mg/mL
Total Product Strength:	1 mg/mL, 2 mg/2 mL, 30 mg/30 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Trevena, Inc.
Panorama #:	2018-24104240
DMEPA Safety Evaluator:	Cameron Johnson, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD

Contents

1	INTRODUCTION	1
1.1	Regulatory History	1
1.2	Product Information	1
2	RESULTS.....	2
2.1	Misbranding Assessment	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS	3
3.1	Comments to the Applicant.....	3
4	REFERENCES	4
	APPENDICES	5

1 INTRODUCTION

This review evaluates the proposed proprietary name, Olinvyk, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Olinvo***, on March 4, 2016 which was found to be conditionally acceptable.^a The Applicant resubmitted the name, Olinvo***, on December 11, 2017 under NDA 210730. However, we found the name, Olinvo*** unacceptable (b) (4)

Thus, the Applicant submitted the name, Olinvyk, for review on June 26, 2018.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on June 26, 2018.

- Intended Pronunciation: oh-LIN-vick
- Active Ingredient: oliceridine
- Indication of Use: management of moderate to severe acute pain in adults for whom an IV opioid is warranted
- Route of Administration: intravenous
- Dosage Form: injection
- Strength: 1 mg/mL
- Dose and Frequency:
 - Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed
 - Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed
- How Supplied: 1mg/mL in 2 mL glass vial, 2mg/2mL in 2 mL glass vial, 30 mg/30 mL in 30 mL glass vial
- Storage: room temperature

^a Shah, M. Proprietary Name Review for Olinvo*** (IND 113537). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 25. Panorama No. 2016-2986617.

^b Johnson, C. Proprietary Name Review for Olinvo*** (NDA 210730). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 MAR 9. Panorama No. 2017-19602967.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 *United States Adopted Names (USAN) Search*

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

2.2.2 *Components of the Proposed Proprietary Name*

The Applicant did not provide a derivation or intended meaning for the proposed name, Olinvyk in their submission. This proprietary name is comprised of a single word that does not contain any 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, July 6, 2018 e-mail, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 *FDA Name Simulation Studies*

Fifty-one practitioners participated in DMEPA's prescription studies. 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 verbal and written prescription studies.

2.2.5 *Phonetic and Orthographic Computer Analysis (POCA) Search Results*

Our POCA search^d identified 18 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.

^c USAN stem search conducted on (6/28/2018).

^d POCA search conducted on (6/27/2018) in version 4.2.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists 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 1. Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	11
Low similarity name pair: combined match percentage score $\leq 54\%$	5

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 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 Anesthesia, Analgesia, and Addiction Products (DAAAP) via e-mail on July 27, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DAAAP on August 3, 2018, they stated no additional concerns with the proposed proprietary name, Olinvyk.

3 CONCLUSION

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Ruth Maduro, OSE project manager, at 240-402-4232.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your submission, received on June 26, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. **USAN Stems** (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

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.[°]

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

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

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

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

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

- 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 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 <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 $\leq 54\%$).

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. Olinvyk Study (Conducted on July 6, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> Olinvyk 1 mg IV every 3 hours as needed	Olinvyk 1 mg/mL Bring to clinic Dispense 1 vial
<u>Outpatient Prescription:</u> Olinvyk 1mg/mL Bring to clinic Disp # 1 vial	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Olinvyk				
305 People Received Study				
51 People Responded				
Total	16	14	21	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
ALINVYK	3	0	0	3
OLEMBIC	0	1	0	1
OLIMVIC	0	1	0	1
OLINDIX	0	1	0	1

OLINOYK	0	0	1	1
OLINVIC	0	4	0	4
OLINVICK	0	1	0	1
OLINVIK	0	2	0	2
OLINVRYK	1	0	0	1
OLINVYK	12	0	20	32
OLYNVIC	0	1	0	1
OLYNVIK	0	1	0	1
VOLINVIC	0	1	0	1
VOLINVIK	0	1	0	1

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

No.	Proposed name: Olinvyk Established name: oliceridine Dosage form: injection Strength(s): 1 mg/mL, 2 mg/2 mL, 30 mg/30 mL Usual Dose: • Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed • Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed	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.	Olinvyk	100	Name is subject of this review.
2.	Olinvo***	74	Proposed proprietary name for NDA 210730 found unacceptable by DMEPA (OSE# 2017-19602967 dated 03/9/2018). A new proposed proprietary name, Olinvyk*** (name subject of this review), has been submitted.

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 (%)
3.	Choline C-11	56
4.	Linzess	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: Olinvyk Established name: oliceridine Dosage form: injection Strength(s): 1 mg/mL, 2 mg/2 mL, 30 mg/30 mL Usual Dose: - Titration: initial intravenous bolus dose of 1 mg to 2 mg; subsequent doses of 1 mg to 2 mg may be given as soon as 15 minutes after the previous dose as needed - Maintenance: bolus doses of 1 mg to 3 mg doses every 1 to 3 hours as needed; use 0.1 mg to 0.5 mg demand doses via PCA as needed	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
5.	(b) (4)	62	This name pair has sufficient orthographic and phonetic differences.
6.	Novolin	46	This name pair has sufficient orthographic and phonetic differences.
7.	Novolin 70/30	46	This name pair has sufficient orthographic and phonetic differences.
8.	Novolin N	46	This name pair has sufficient orthographic and phonetic differences.
9.	Palynziq	56	This name pair has sufficient orthographic and phonetic differences.
10.	Ozempic	50	This name pair has sufficient orthographic and phonetic differences.
11.	Blinicyto	56	This name pair has sufficient orthographic and phonetic differences.
12.	(b) (4)	60	This name pair has sufficient orthographic and phonetic differences.
13.	V-Cillin K	56	This name pair has sufficient orthographic and phonetic differences.
14.	Zolinza	59	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 (%)
-----	------	----------------

No.	Name	POCA Score (%)
	N/A	

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
15.	Novolin L	50	Brand discontinued with no generic equivalent available. (b) (4) (b) (4)
16.	Olivine	58	Product is not a drug. It is a rock-forming mineral.

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 (%)
17.	Ivy Block	56
18.	Lanozin	55

^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

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/

CAMERON D JOHNSON
08/06/2018

OTTO L TOWNSEND
08/06/2018

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:	March 9, 2018
Application Type and Number:	NDA 210730
Product Name and Strength:	Olinvo (oliceridine) injection, 1 mg/mL
Total Product Strength:	1 mg/1 mL, 2 mg/2 mL, 30 mg/30 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Trevena, Inc.
Panorama #:	2017-19602967
DMEPA Safety Evaluator:	Cameron Johnson, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD
DMEPA Deputy Director (Acting):	Danielle Harris, PharmD, BCPS
DMEPA Director:	Todd Bridges, RPh

Contents

1	INTRODUCTION	1
1.1	Regulatory History	1
1.2	Product Information	1
2	RESULTS.....	1
2.1	Misbranding Assessment	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS	3
3.1	Comments to the Applicant.....	4
4.	REFERENCES	6
	APPENDICES	7

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Olinvo, on March 4, 2016 under IND 113537. Olinvo was determined to be conditionally acceptable on April 25, 2016 in OSE Review # 2016-2986617^a.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 11, 2017 proprietary name submission.

- Intended Pronunciation: oh-LIN-voh
- Active Ingredient: oliceridine
- Indication of Use: For the management of moderate to severe acute pain in adult patients for whom an intravenous (IV) opioid is warranted
- Route of Administration: intravenous
- Dosage Form: injection
- Strength: 1 mg/1 mL, 2 mg/2 mL, 30 mg/30 mL
- Dose and Frequency: initial dose of 1 mg to 3 mg with subsequent doses given every 10 minutes as needed based on patient need; maintenance doses of 1 mg to 3 mg every 1 to 3 hours as needed or as patient-controlled analgesia (PCA) demand doses of 0.1 mg to 0.5 mg as needed
- How Supplied: available as 1 mg/mL in a 2 mL glass vial; 2 mg/ 2 mL in 2 mL glass vial; 30 mg /30 mL in 30 mL glass vial
- Storage: room temperature; do not freeze; protect from light

2 RESULTS

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

^a Shah, Millie, Proprietary Name Review for Olinvo*** (IND 113537). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 APR 25. OSE RCM No. 2016-2986617.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Olinvo, in their submission. This proprietary name is comprised of a single word that does not contain any 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, December 20, 2018 e-mail, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred three (103) practitioners participated in DMEPA's prescription studies. In the written inpatient prescription study one participant misinterpreted Olinvo as "Olizio". The name "Olizio" sounds like the marketed drug "Olysio". Our analysis of the name pair, Olinvo and Olysio, determined that the risk of confusion will be mitigated based on the orthographic, phonetic and product characteristic differences. Orthographically, the infixes of the name pair "-lys-" vs. "-lin-" look different because Olysio has one downstroke "y" in the third position while Olinvo has an "i" in the third position. Phonetically, the names have a different number of syllables and the third syllable in Olysio, "see", sounds different from the third syllable in Olinvo "oh". Additionally, Olinvo and Olysio have different strengths (1 mg / 1 mL, 2 mg/ 2 mL, 30 mg/ 30 mL vs. 150 mg), formulations (injection vs. capsule), route of administration (intravenous vs. oral) and frequency of administration (as needed based on patient need vs. once daily). See Appendix E for our assessment of the name pair. Appendix B contains the results from the verbal and written prescription studies.

^b USAN stem search conducted on (01/08/2018).

2.2.5 *Phonetic and Orthographic Computer Analysis (POCA) Search Results*

Our POCA search^c identified 55 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, FDA Prescription Simulation Study, and the (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. 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 $\leq 69\%$	40
Low similarity name pair: combined match percentage score $\leq 54\%$	23

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

We determined 63 of the 64 names will not pose a risk for confusion as described in Appendices C through H. However, the proposed name could be confused with (b) (4). The rationale for the risk of confusion is described in Section 3.1.

2.2.8 *Communication of DMEPA's Analysis at Midpoint of Review*

DMEPA communicated our findings to the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) via e-mail on March 8, 2018. At that time, we also requested additional information or concerns that could inform our review. The division did not respond with any additional concerns with the proposed proprietary name.

3 CONCLUSIONS

The proposed proprietary name is not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with (b) (4). Therefore, the decision to deny the name will be communicated to the Applicant/Sponsor via letter (See *Section 3.1*).

If you have further questions or need clarifications, please contact Corwin Howard, OSE project manager, at 301-796-8654.

^c POCA search conducted on (01/08/2018) in version 4.2.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Olinvo, and have concluded that this name is unacceptable for the following reasons:

(b) (4)



1 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

4. REFERENCES

1. **USAN Stems** (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

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.

3. *Electronic Drug Registration and Listing System (eDRLS) database*

The electronic Drug Registration and Listing System (eDRLS) was established to support the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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.^h

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

***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 namesⁱ. 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.,

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

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 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.

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

- 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 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
--------	--

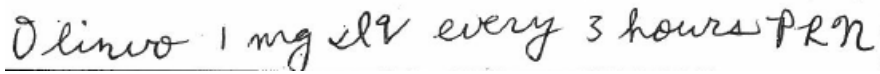
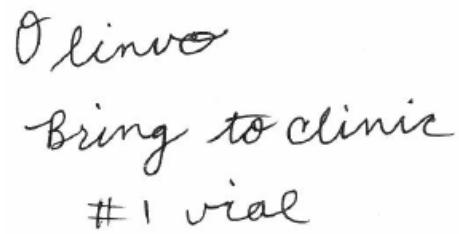
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.		
	<table> <tr> <td data-bbox="298 369 883 1281"> 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? </td><td data-bbox="883 369 1360 1281"> 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 <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 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 <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 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 $\leq 54\%$).

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. Olinvo Study (Conducted on 01/03/2018)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Olinvo Bring to clinic Dispense 1 vial
<u>Outpatient Prescription:</u> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Olinvo

293 People Received Study

103 People Responded

Total	38	27	38	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
OLENBO	0	1	0	1
OLENVO	0	1	0	1
OLIMBO	0	7	0	7
OLINBO	0	1	0	1
OLINBOW	0	1	0	1

OLINDO	0	1	0	1
OLINERO	0	0	1	1
OLINVO	37	13	36	86
OLIVNO	1	0	0	1
OLIZIO	0	0	1	1
OLYMBO	0	1	0	1
OLYNVO	0	1	0	1

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

No.	Proposed name: Olinvo Established name: oliceridine Dosage form: injection Strength(s): 1 mg/ 1 mL, 2 mg/2 mL, 30 mg/ 30 mL Usual Dose: initial dose of 1 mg to 3 mg with subsequent doses given every 10 minutes as needed based on patient need; maintenance doses of 1 mg to 3 mg every 1 to 3 hours as needed or as patient-controlled analgesia (PCA) demand doses of 0.1 mg to 0.5 mg as needed	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.	Olinvo	100	Name 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 (%)
2.	Lanolin	54
3.	Lanolin Oil	48 ortho: 72
4.	Linzess	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: Olinvo Established name: oliceridine Dosage form: injection Strength(s): 1 mg /1 mL, 2 mg/2 mL, 30 mg/30 mL Usual Dose: initial dose of 1 mg to 3 mg with subsequent doses given every 10 minutes as needed based on patient need; maintenance doses of 1 mg to 3 mg every 1 to 3 hours as needed or as patient-controlled analgesia (PCA) demand doses of 0.1 mg to 0.5 mg as needed	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
5.	Novolin	55	This name pair has sufficient orthographic and phonetic differences.
6.	Novolin 70/30	55	This name pair has sufficient orthographic and phonetic differences.
7.	Novolin N	54	This name pair has sufficient orthographic and phonetic differences
8.	Livalo	60	This name pair has sufficient orthographic and phonetic differences.
9.	Novolin R	54	This name pair has sufficient orthographic and phonetic differences.
10.	Evoclin	51	This name pair has sufficient orthographic and phonetic differences.

11.	(b) (4)	66	This name pair has sufficient orthographic and phonetic differences.
12.	Dolono	63	This name pair has sufficient orthographic and phonetic differences.
13.	Myolin	56	This name pair has sufficient orthographic and phonetic differences.
14.	Relion/ Novolin 70/30	49	This name pair has sufficient orthographic and phonetic differences.
15.	Floxin IV	48	This name pair has sufficient orthographic and phonetic differences.
16.	Livostin	46	This name pair has sufficient orthographic and phonetic differences.
17.	Ventolin	46	This name pair has sufficient orthographic and phonetic differences.
18.	Molindone	56	This name pair has sufficient orthographic and phonetic differences.
19.	Relion/Novolin N	48	This name pair has sufficient orthographic and phonetic differences.
20.	Ellence	55	This name pair has sufficient orthographic and phonetic differences.
21.	(b) (4)	62	This name pair has sufficient orthographic and phonetic differences.
22.	Zolinza	68	Orthographically the names begin with different first letters “O” vs. “Z” which look different when scripted. This makes the prefixes of the name pair “O” vs. “Zo” look different. Phonetically the first and last syllables of the name pair sound different (Zo vs. O and “zah” vs. “voh”). Product Characteristic Differences: • Strength and formulation: Olinvo is available as an intravenous vial with multiple strengths (1 mg/ 1 mL, 2 mg/ 2 mL, 30 mg/ 30 mL) while Zolinza is available as a single strength 100 mg capsule. • Route of Administration: Olinvo is given by the intravenous route while Zolinza is given by the oral route. • Frequency of Administration: Olinvo is dosed as needed every 10 minutes to every 1 to 3 hours based on individual patient need while Zolinza is dosed once daily with food.
23.	Oleptro	55	This name pair has sufficient orthographic and phonetic differences.
24.	Olysio	59	Orthographically the infixes of the name pair “-lys-” vs. “-lin-” look different because Olysio has one

			downstroke “y” in the third position while Olinvo has an “i” in the third position. Phonetically the names have a different number of syllables and the third syllable in Olysio (“see”) sounds different from the third syllable in Olinvo (“oh”) Product Characteristic Differences: • Strength and formulation: Olinvo is available as an intravenous vial in multiple strengths (1 mg/1 mL, 2 mg/2 mL, 30 mg/30 mL) while Olysio is available as a single strength capsule (150 mg). • Route of Administration: Olinvo is given by the intravenous route while Olysio is given by the oral route. • Frequency of Administration: Olinvo is dosed as needed every 10 minutes to every 1 to 3 hours based on individual patient need while Olysio is dosed once daily.
25.	Opdivo	55	This name pair has sufficient orthographic and phonetic differences.
26.	(b) (4)	56	This name pair has sufficient orthographic and phonetic differences.
27.	Clinpro 5000	56	This name pair has sufficient orthographic and phonetic differences.
28.	Nolix	58	This name pair has sufficient orthographic and phonetic differences.
29.	(b) (4)	56	This name pair has sufficient orthographic and phonetic differences.
30.	Xolido	62	This name pair has sufficient orthographic and phonetic differences.
31.	(b) (4)	62	This name pair has sufficient orthographic and phonetic differences.
32.	Avinza	55	Orthographically the prefixes of this name pair “Ol” vs “Av” look different because Olinvo has an upstroke “l” in the 2nd position while Avinza has a “v” in the 2nd position. Phonetically the last syllables of the name pair sound different (“voh” vs. “zah”) due to differences in pronunciation of “v” vs. “z”.
33.	Ilevro	60	Phonetically the first and second syllables of the name pair sound different “oh” vs. “i”, and “lin” vs. “lev”. Product characteristic differences: • Strength: Olinvo is available as an intravenous vial with multiple strengths (1 mg/1 mL, 2 mg/2 mL, 30 mg/30 mL) while Ilevro is available as a single strength ophthalmic suspension (0.3%).

			- Route of Administration: Olinvo is given by the intravenous route while Ilevro is given by the ophthalmic route. - Frequency of Administration: Olinvo is dosed as needed every 10 minutes to every 1 to 3 hours based on individual patient need while Ilevro is dosed once daily.
--	--	--	--

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

No.	Name	POCA Score (%)
34.	Alimta	50
35.	Boniva	50
36.	Lenvima	54
37.	Odomzo	52
38.	Olux E	52
39.	Onglyza	42
40.	Onsolis	42
41.	Orlistat	40
42.	Relenza	48

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
43.	Novolin L	58	Brand discontinued with no generic equivalent available. NDA 018777 withdrawn from FR effective 06/05/1996 and NDA 019965 withdrawn FR effective date 03/13/2009.
44.	Olive Oil	58	Product is not a drug. It is an oil derived from olives and used in cooking.
45.	Olivine	63	Product is not a drug. It is a rock-forming mineral.
46.	(b) (4)	48	This is an alternate proposed proprietary name for NDA 201739 and NDA 201739 was approved under proprietary name Auvi-Q.
47.	Linalool, (-)-	58	This is not a drug. This is a chemical compound found in flowers and plants and often used to add a scent to perfumes, lotions and soaps.
48.	Linalool, (+)-	58	This is not a drug. This is a chemical compound found in flowers and plants and often used to add a scent to perfumes, lotions and soaps.

No.	Name	POCA Score (%)	Failure preventions
49.	Linalool, (+-)-	58	This is not a drug. This is a chemical compound found in flowers and plants and often used to add a scent to perfumes, lotions and soaps.
50.	Linalool, (-)-	58	This is not a drug. This is a chemical compound found in flowers and plants and often used to add a scent to perfumes, lotions and soaps.
51.	Kaolin	56	This product is a chemical used for compounding. As a drug, it is only available as a veterinary product.
52.	Solian	56	International amisulpride product marketed in many countries.
53.	Bisolvon	46 Ortho: 71	International product marketed in many foreign countries.
54.	(b) (4)	50	Proposed proprietary name for NDA 202810 found unacceptable by DMEPA (OSE#2012-373). NDA 202810 approved under new proprietary name Oxtellar XR.
55.	Refolinon	50	International product marketed in Greece, South Africa and United Kingdom.
56.	Clinsol	60	Veterinary product
57.	Linde	61	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

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

No.	Name	POCA Score (%)
58.	Allanfol	59

^j 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

No.	Name	POCA Score (%)
59.	Dalimzo	60
60.	Inzo	58
61.	Slo-Indo	60
62.	Tlando	58
63.	Vimovo	60

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CAMERON D JOHNSON
03/09/2018

OTTO L TOWNSEND
03/09/2018

DANIELLE M HARRIS
03/09/2018

TODD D BRIDGES
03/09/2018