CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217686Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME MEMORANDUM

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

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

Date of This Review:	March 14, 2024
Application Type and Number:	IND 122772 and NDA 217686
Product Name, Dosage Form, and Strength:	Tryvio (aprocitentan) tablet, 12.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Idorsia Pharmaceuticals Ltd (Idorsia)
PNR ID #:	2022-1044724390-1 and 2022-1044724894-1
DMEPA 2 Safety Evaluator:	Jody Kundreskas, PharmD
DMEPA 2 Team Leader (Acting):	Nicole Iverson, PharmD, BCPS
DMEPA 2 Associate Director for Nomenclature & Labeling:	Hina Mehta, PharmD

1 INTRODUCTION

This memorandum is initiated by DMEPA 2 to reassess the proposed proprietary name, Tryvio, to evaluate the change in (b) (4) Previously, the proposed proprietary name, Tryvio, was found conditionally acceptable under IND 122772 and NDA 217686 as 12.5 mg (b) (4) tablets on March 10, 2023.[a] However, during the review cycle, the Division of Cardiology and Nephrology (DCN) determined that (b) (4).

2 DISCUSSION

2.1 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, Tryvio, we evaluated the previously identified names taking into account the change in (b) (4). Our evaluation has not altered our previous conclusion regarding the acceptability of the proposed proprietary name, Tryvio.

Additionally, we searched the USAN stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The March 5, 2024 search of USAN stems did not find any USAN stems in the proposed proprietary name, Tryvio.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Tryvio, is conditionally acceptable.

[a] Kundreskas, J. Proprietary Name Review for Tryvio (IND 122772 and NDA 217686). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 MAR 10. PNR ID Nos. 2022-1044724390 and 2022-1044724894.

4 REFERENCE

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

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

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/

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PROPRIETARY NAME REVIEW

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

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Date of This Review:	March 10, 2023
Application Type and Number:	IND 122772 and NDA 217686
Product Name and Strength:	Tryvio (aprocitentan) tablet, 12.5 mg (b) (4)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Idorsia Pharmaceuticals Ltd (Idorsia)
PNR ID #:	2022-1044724390 and 2022-1044724894
DMEPA 2 Safety Evaluator:	Jody Kundreskas, PharmD
DMEPA 2 Team Leader:	Hina Mehta, PharmD
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Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tryvio, 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. Idorsia did not submit an external name study for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on January 11, 2022 under IND 122772, and December 19, 2022 under NDA 217686.

- Intended Pronunciation: try vee' oh
- Active Ingredient: aprocitentan
- Indication of Use: treatment of hypertension, to lower blood pressure in patients who are not adequately controlled on other drugs
- Route of Administration: oral
- Dosage Form: tablet
- Strength: 12.5 mg (b) (4)
- Dose and Frequency: 12.5 mg orally once daily. (b) (4)
- How Supplied: 12.5 mg (b) (4) tablets are available in a hospital unit dose blister of 10 tablets and a bottle of 30 with child-resistant closure.
- Storage: Store at 20ºC to 25ºC (68ºF to 77ºF); excursions permitted from 15ºC to 30ºC (59ºF to 86ºF) [see USP Controlled Room Temperature]. Store in the original package. Protect from light and moisture.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[a].

2.2.2 Components of the Proposed Proprietary Name

Idorsia did not provide a derivation or intended meaning for the proposed proprietary name, Tryvio, in their submission. This proprietary name is comprised of a single word that contains the letter string "TR" which is a medical abbreviation for "time release." Although we typically discourage the inclusion of medical abbreviations in proprietary names, we note the letter string "TR" is a common letter string in existing drug nomenclature (e.g., Adcetris, Entresto, Myrbetriq, Tracleer, Tradjenta, Trazimera, Treanda, Trelegy, Trulicity, etc.) and we are unaware of post-market reports of medication errors associated with this specific abbreviation through our routine surveillance. We also evaluated the potential risk of misinterpreting the proposed proprietary name as "TR [drug name similar to YVIO]" and did not identify any concerns[b]. Therefore, in this case we do not object to the proposed proprietary name based on the inclusion of this medical abbreviation. Tryvio does not contain any other components (i.e. a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On February 7, 2023, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Tryvio at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-three practitioners participated in FDA's prescription simulation studies for Tryvio.

Seven participants in the inpatient study misinterpreted the study name Tryvio as "Tryvis" which is a close variation to the marketed product "Trivisc". Additionally, twelve participants in the voice study misinterpreted the name as "Trivio" or "Tri-Vio" which are close variations to an unapproved marketed product Trivix. We evaluated the name pairs Tryvio vs. Trivisc and Tryvio vs. Trivix in Appendix E and determined that there are sufficient orthographic and phonetic differences and distinguishing product characteristics to reduce the likelihood of name confusion.

The remaining study responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[c] identified 91 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

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[a] USAN stem search conducted on December 23, 2022.

[b] POCA search conducted on December 30, 2022 in version 5.2.

[c] POCA search conducted on December 23, 2022 in version 5.2.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

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

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	90
Low similarity name pair: combined match percentage score ≤54%	0

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

Our analysis of the 92 names contained in Table 1 determined none of the names will pose a risk for confusion with Tryvio as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On March 10, 2023, DMEPA 2 communicated our determination to the Division of Cardiology and Nephrology (DCN).

3 CONCLUSION

The proposed proprietary name, Tryvio, is conditionally acceptable.

If you have any questions or need clarifications, please contact Monique Killen, OSE project manager, at 240-402-1985.

3.1 COMMENTS TO IDORSIA PHARMACEUTICALS LTD

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

If any of the proposed product characteristics as stated in your submission, received on December 19, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [d]

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

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

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

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

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤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[e]. 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

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

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

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

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

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

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

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

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

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

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

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

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

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

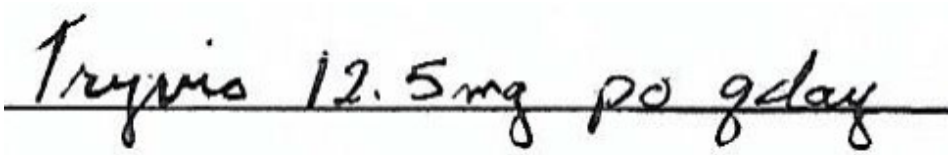
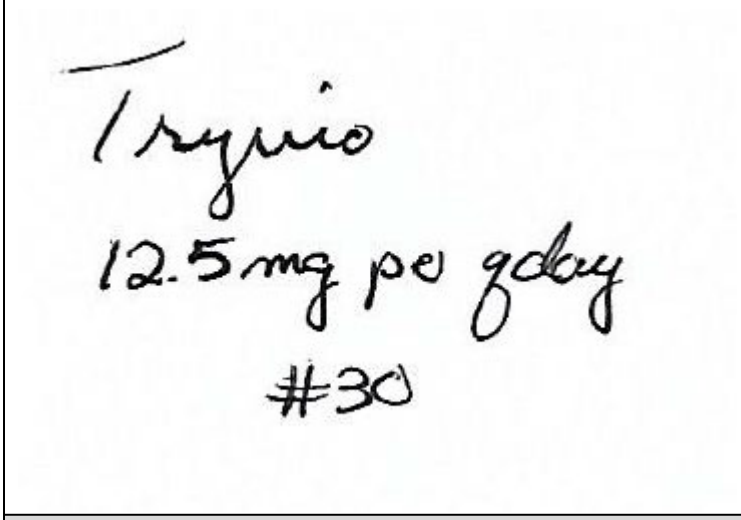
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or 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 ≤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. Tryvio Study (Conducted on study date)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Tryvio Take 12.5 mg by mouth once daily Dispense #30
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Tryvio	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Tryvio

259 People Received Study

93 People Responded

Total	25	22	24	22	93

INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
TRIVEO	0	0	2	0	2
TRIVIO	0	0	11	0	11
TRI-VIO	0	0	1	0	1
TRYRIS	1	0	0	0	1
TRYVEO	0	0	1	0	1
TRYVIO	17	22	9	22	70
TRYVIS	7	0	0	0	7

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

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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.	Tryvio***	100	This proposed proprietary name is the subject of this review.
2.	Travivo***	77	Proposed proprietary name for IND 033626 found unacceptable by DMEPA (OSE# 2019-30639998 dated October 1, 2019) due to confusion with a marketed product, Tarceva. Subsequently, the proposed proprietary name Exxua*** was found conditionally acceptable for IND 033626.

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

No.	Name	POCA Score (%)
1.	Entyvio	63
2.	Tyvaso	62
3.	Triavil 2-10	61
4.	Triavil 4-10	61
5.	(b) (4)***	60
6.	Zoryve	60
7.	Tridil	59
8.	(b) (4)***	58
9.	Prevduo***	56
10.	Travasol	56
11.	Travasol 10	56
12.	Trilyte	56
13.	Tri-Otic	56

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

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Tri-Vi-Sol	68	Orthographically, these two names differ in length (6 vs. 8 letters). The downstroke y in Tryvio versus the lack of downstrokes in Tri-Vi-Sol plus an upstroke l provide differences. Phonetically, the last syllable provides some differences ('oh' vs. 'sol'). These products differ in strength (12.5 mg (b) (4) vs. 35 mg/1500 units/ 400 units [10 mcg] per 1 mL). We note that Tri-Vi-Sol has one strength, which may be omitted on an order. Dosages for these products may share numerical similarity but differ in unit (1 tablet vs. 1 mL). (b) (4) The name pair differ in dosage form (tablet vs. solution).
2.	Trivora-28	68	Orthographically, the downstroke y in Tryvio versus lack of downstrokes in Trivora-28 provide some differences. In addition, Trivora has a modifier '28' which if included can provide some differences. Phonetically, the ending sounds of the middle syllable ('vee' vs. 'vor') and the last syllable ('oh' vs. 'ah') provide some differences.

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
			These products differ in overall strength with one numerical similarity (12.5 mg (b) (4) vs. a triphasic 0.05 mg/0.03 mg, 0.075 mg/0.04 mg, 0.125 mg/0.03 mg and placebo). We note most orders for Trivora-28 will not include the triphasic strengths and therefore may overlap in dose with Tryvio (1 tablet). (b) (4) When all of the aforementioned factors are considered in totality, we find the risk of name confusion between the name pair is adequately minimized in this case.
3.	Trivora	68	Orthographically, the downstroke y in Tryvio versus lack of downstrokes in Trivora provide some differences. In addition, Trivora has a modifier '28' which if included can provide some differences. Phonetically, the ending sounds of the middle syllable ('vee' vs. 'vor') and the last syllable ('oh' vs. 'ah') provide some differences. These products differ in overall strength with one numerical similarity (12.5 mg (b) (4) vs. a triphasic 0.05 mg/0.03 mg, 0.075 mg/0.04 mg, 0.125 mg/0.03 mg and placebo). We note

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
			most orders for Trivora will not include the triphasic strengths and therefore may overlap in dose with Tryvio (1 tablet). (b) (4) When all of the aforementioned factors are considered in totality, we find the risk of name confusion between the name pair is adequately minimized in this case.
4.	Triveen	64	This name pair has sufficient orthographic and phonetic differences.
5.	Trivix	64	Orthographically, the downstroke y in Tryvio versus lack of downstrokes in Trivix and ending letters (o vs x) provide some differences. Phonetically, Tryvio contains an extra syllable and the last syllables ('oh' vs. 'vicks') provide sufficient differences. These products differ in overall strength with no numerical similarity (12.5 mg (b) (4) vs. 0.1%/5%), although we acknowledge that Trivix is a single strength product and strength may not be present on an order. We note that these products also differ in route (oral vs. topical), dosage form (tablet vs. cream), and frequency (once daily vs. two to four times daily).

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
6.	Tri-Sudo	62	This name pair has sufficient orthographic and phonetic differences.
7.	Trilog	62	This name pair has sufficient orthographic and phonetic differences.
8.	Triavil	61	This name pair has sufficient orthographic and phonetic differences.
9.	Triavil 2-25	61	This name pair has sufficient orthographic and phonetic differences.
10.	Triavil 4-25	61	This name pair has sufficient orthographic and phonetic differences.
11.	Triavil 4-50	61	This name pair has sufficient orthographic and phonetic differences.
12.	Tricor	61	Orthographically, the downstroke y in Tryvio versus lack of downstrokes in Tricor, and the suffixes provide some differences. Phonetically, Tryvio contains an extra syllable and the last syllables ('oh' vs. 'core') provide sufficient differences. While these name pairs share some product characteristics (possible dose of 1 tablet, oral route, and once daily frequency) (b) (4) and these strengths do not overlap (12.5 mg (b) (4) vs. 48 mg and 145 mg). When all of the aforementioned factors are considered in totality, we find the risk of name confusion between the name pair is adequately minimized in this case.

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
13.	Trivisc	61	Orthographically, the downstroke y in Tryvio versus lack of downstrokes in Trivisc provide some differences. Phonetically Tryvio contains an extra syllable, and the ending sounds of the last syllable ('sk' vs. 'oh') provide sufficient differences. (b) (4) these products differ in route (oral vs. intraarticular), frequency (once daily vs. once a week for 3 weeks) and dosage form (tablet vs. injection). Additionally, Trivisc is not approved by the FDA as a drug, it is approved as a medical device. As such, in healthcare systems, this product may be ordered and stocked by Central Supply/Logistics rather than pharmacy service. When all of the aforementioned factors are considered in totality, we find the risk of name confusion between the name pair is adequately minimized in this case.
14.	Trizivir	61	Orthographically, these two name pairs differ in length (6 letters vs. 8 letters). The 'z' in Trizivir may be written with a downstroke or without; if written without a downstroke, this provides some orthographic differences. The

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
			ending letter ('o' vs. 'r') also provides some differences. This name pair has sufficient phonetic differences. While these name pairs share some product characteristics (possible dose of 1 tablet, oral route, and dosage form), (b) (4) differ from Trizivir's strength. Since Trizivir (300 mg/150 mg/300 mg) is only available in one strength, this may be omitted on a prescription. Additionally, the frequency differs between these products (daily versus twice daily). When all of the aforementioned factors are considered in totality, we find the risk of name confusion between the name pair is adequately minimized in this case.
15.	Provil	60	This name pair has sufficient orthographic and phonetic differences.
16.	Tri-Nymyo	60	This name pair has sufficient orthographic and phonetic differences.
17.	Tri-Zel	60	This name pair has sufficient orthographic and phonetic differences.
18.	Turalio	60	This name pair has sufficient orthographic and phonetic differences.
19.	Reyvow	58	This name pair has sufficient orthographic and phonetic differences.
20.	Tresiba	58	This name pair has sufficient orthographic differences.

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
			Phonetically the ending of the first syllables differ ('try' vs. 'tray'). The beginning of the second syllables ('vee' vs. 'see') differ as the labiodental affricate /v/ sound differs slightly from the alveolar affricate sound /s/. The third syllable ('oh' vs. 'ba') provide sufficient phonetic differences. Although Tryvio and Tresiba share (b) (4) frequency (once daily), the products do not overlap in strength (12.5 mg (b) (4) vs. U100 or U200), route (oral vs. subcutaneous), and dosage form (tablet vs. injection).
21.	Uptravi	58	This name pair has sufficient orthographic and phonetic differences.
22.	Retrovir	56	This name pair has sufficient orthographic and phonetic differences.
23.	Revatio	56	This name pair has sufficient orthographic and phonetic differences.
24.	Tri-Mili	56	This name pair has sufficient orthographic and phonetic differences.
25.	Relyvrio	56	Orthographically, these two name pairs differ in length (6 letters vs. 8 letters). The beginning letter ('T' vs. 'R') and upstroke 'l' in Relyvrio provides some orthographic differences. This name pair has sufficient phonetic differences.

No.	**Proposed name:** Tryvio **Established name:** aprocitentan **Dosage form:** tablet **Strength(s):** 12.5 mg (b) (4) **Usual Dose:** 12.5 mg orally once daily. (b) (4)	**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**
			While these name pairs share some product characteristics (possible dose of 1 tablet vs. 1 packet, and oral route), (b) (4) do not overlap with Relyvrio (available in a combination 3 gram/1 gram powder). Since Relyvrio is only available in one strength, this may be omitted on a prescription. Additionally, the frequency may differ between these products (daily versus once daily titrated to twice daily after 3 weeks).
26.	Revia	56	This name pair has sufficient orthographic and phonetic differences.
27.	Trimox	56	This name pair has sufficient orthographic and phonetic differences.
28.	Triofed	56	This name pair has sufficient orthographic and phonetic differences.
29.	Triphed	56	This name pair has sufficient orthographic and phonetic differences.
30.	(b) (4) ***	56	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
1.	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
1.	Trivora-21	68	Brand discontinued with no generic equivalents available. Product is available only as Trivora-28 (reviewed in another appendix)
2.	Otrivin	65	Name identified in RxNorm database. Per Redbook, product is deactivated with no generic equivalents available.
3.	(b) (4) ***	65	Proposed proprietary name for IND 104839 found to be unacceptable (OSE RCM# 2016-8807820). The product was later approved under the proprietary name, Xerava and is currently marketed under that name (NDA 211109).
4.	Tritop	64	Veterinary product
5.	(b) (4) ***	62	(b) (4)
6.	Trysul	61	Brand discontinued with no generic equivalents available. ANDA 087887 withdrawn FR effective 12/07/2007.
7.	Otrivine	60	International product
8.	(b) (4) ***	60	Proposed proprietary name for IND 137856 found unacceptable by DMEPA (OSE# 2020-1043779388). NDA 216264 approved under the proprietary name Bludigo and is currently marketed under that name.
9.	(b) (4) ***	60	Proposed proprietary name for IND (b) (4) found unacceptable by DMEPA (OSE# 2016-915271 dated February 9, 2017). BLA 761289 approved under the proprietary name Imjudo and is currently marketed under that name.
10.	Trivase	60	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
11.	Trovan	59	All Trovan brands discontinued with no generic equivalents available. NDAs 020759, 020760 withdrawn FR effective 06/16/2006 and NDA 050762 withdrawn FR effective 09/22/1999
12.	Travenol	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
13.	Trivaris	58	Brand discontinued with no TE codes provided per Drugs@FDA database, and NDA 022220 is withdrawn FR effective July 21, 2017.

No.	Name	POCA Score (%)	Failure preventions
14.	(b) (4) ***	58	Proposed proprietary name for IND 118313 found unacceptable by DMEPA (OSE# 2018-22563733 dated 10/18/2018). NDA 212122 approved under the proprietary name Breztri Aerosphere and is currently marketed under that name.
15.	Trynate	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
16.	(b) (4) ***	57	This is an alternate proposed proprietary name for IND 147753 and NDA 214787 was approved under proprietary name Veklury and is currently marketed under that name.
17.	Trovan Iv	57	All Trovan brands discontinued with no generic equivalents available. NDAs 020759, 020760 withdrawn FR effective 06/16/2006 and NDA 050762 withdrawn FR effective 09/22/1999
18.	Trypsin	57	This product is not a finished drug. It is a bulk powder used for compounding.
19.	Privine	56	Name identified in RxNorm database. Per Redbook, product is deactivated with no generic equivalents available.
20.	Revitol	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Trasicor	56	Brand discontinued with no generic equivalents available. NDA 018166 withdrawn FR effective 09/29/1995.
22.	Travasol 2.75	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
23.	Travasol 2.75/5	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
24.	Travasol 3.5	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
25.	Travasol 4.25/10	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
26.	Travasol 4.25/25	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.

No.	Name	POCA Score (%)	Failure preventions
27.	Travasol 4.25/5	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
28.	Travasol 5.5	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
29.	Travasol 8.5%	56	All the Travasol products have been discontinued (no generics available) except for Travasol 10, which is separately evaluated.
30.	Tri-Dec	56	Name identified in RxNorm database. Product is deactivated per Red Book with no generic equivalents available.
31.	Tridione	56	Brand discontinued with no generic equivalents available. NDA 005856 withdrawn FR effective 09/15/2022.
32.	Trilone	56	Name identified in RxNorm database. Product is deactivated per Red Book with no generic equivalents available.
33.	(b) (4) ***	56	Name identified as name entered by safety evaluator. Unable to find product characteristics in commonly used drug databases
34.	(b) (4) ***	55	Proposed proprietary name for IND 123087 found unacceptable (OSE# 2020-38213033 dated August 10, 2020). NDA 215014 approved under the proprietary name Empaveli and is currently marketed under that name.
35.	Triban	55	Name identified in RxNorm database. Per Redbook, product is deactivated with no generic equivalents available.
36.	Tropium	55	International product
37.	Trosyl	55	International product

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

No.	Name	POCA Score (%)
1.	Crysti-12	60
2.	Crysvita	60

[f] 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 (%)
3.	Abrysvo***	56
4.	(b) (4)***	56
5.	(b) (4)***	56
6.	Drysol	56
7.	(b) (4)***	56
8.	Apriso	55
9.	Brevicon	55
10.	Bridion	55

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/s/

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