CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022231Orig1s000

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:	July 28, 2022
Application Type and Number:	NDA 022231
Product Name and Strength:	Terlivaz (terlipressin) for injection, 0.85 mg per vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Mallinckrodt Pharmaceuticals, Inc. (Mallinckrodt)
PNR ID #:	2022-1044724625
DMEPA 2 Safety Evaluator:	Devin Kane, PharmD
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Deputy Director (Acting):	Chi-Ming (Alice) Tu, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Terlivaz, which was found conditionally acceptable under NDA 022231 on November 3, 2021.[a] On February 18, 2022, NDA 022231 received a complete response letter. Thus, Mallinckrodt submitted a response to the complete letter on June 9, 2022 and included the request for review of the name, Terlivaz, under NDA 022231. We note that all product characteristics remain the same.

2 METHODS AND DISCUSSION

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Terlivaz 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 Terlivaz. The Division of Cardiology and Nephrology (DCN) concurred with the findings of OPDP's assessment for Terlivaz.

2.2 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, we 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 proposed proprietary name. Our reassessment did not change our conclusion regarding the previously identified names of concern. Additionally, we searched the United States Adopted Name (USAN) stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The June 28, 2022 search of USAN stems did not find any USAN stems in the proposed proprietary name, Terlivaz.

2.3 COMMUNICATION OF DMEPA'S DETERMINATION

On July 28, 2022, we communicated our determination to the Division of Cardiology and Nephrology (DCN).

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, Terlivaz, is acceptable.

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

3.1 COMMENTS TO MALLINCKRODT PHARMACEUTICALS, INC.

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

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[a] Kane, D. Proprietary Name Review for Terlivaz (NDA 022231). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 NOV 03. PNR ID No. 2021-1044724138.

If any of the proposed product characteristics as stated in your submission, received on June 9, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCE

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

   USAN Stems List contains all the recognized USAN 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/

DEVIN R KANE
07/28/2022 09:43:27 AM

HINA S MEHTA
07/29/2022 03:23:20 PM

CHI-MING TU
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PROPRIETARY NAME REVIEW

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

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

Date of This Review:	November 3, 2021
Application Type and Number:	NDA 022231
Product Name and Strength:	Terlivaz (terlipressin) for injection, 0.85 mg per vial (equivalent to 1 mg of terlipressin acetate)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Mallinckrodt Pharmaceuticals, Inc. (Mallinckrodt)
PNR ID #:	2021-1044724138
DMEPA 2 Safety Evaluator:	Devin Kane, PharmD
DMEPA 2 Team Leader:	Hina Mehta, PharmD
272DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Terlivaz, 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. Mallinckrodt submitted an external name study, conducted by [redacted] (b) (4) for this proposed proprietary name.

1.1 REGULATORY HISTORY

Many Applicants/Sponsors have been involved in the development of the proposed terlipressin for injection. DMEPA previously evaluated the proposed proprietary name, Lucassin***, for this product from the former Applicant Orphan Therapeutics, LLC and found the name conditionally acceptable under NDA 022231, but the application received a Completed Response in 2009. Eventually, the name, Lucassin***, was withdrawn by Ikaria Inc. in 2013.

The former Sponsor Ikaria Inc. previously submitted the proposed proprietary name, Terlivaz, on March 28, 2013. We found the name, Terlivaz, acceptable under IND 068582 on September 17, 2013.[a]

The former Sponsor INO Therapeutics, LLC resubmitted the name, Terlivaz, for review on August 22, 2018. We found the name, Terlivaz, acceptable under IND 068582 on January 17, 2019.[b]

The current Applicant Mallinckrodt submitted the name, Terlivaz, for review on March 12, 2020. We found the name, Terlivaz, acceptable under NDA 022231 on April 23, 2020.[c]

On September 11, 2020, NDA 022231 received a complete response letter. Thus, on August 18, 2021 Mallinckrodt submitted a response to the complete response letter and included the request for review of Terlivaz*** under NDA 022231. We note that all product characteristics remain the same.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 18, 2021.

- Intended Pronunciation: TUR-lih-vaz
- Active Ingredient: terlipressin
- Indication of Use: The proposed indication is to treat patients with hepatorenal syndrome (HRS) Type 1.

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[a] DeFronzo, K. Proprietary Name Review for Terlivaz (IND 68582). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 Sep 17. Panorama No. 2013-830.

[b] Straka, M. Proprietary Name Review for Terlivaz (IND 68582). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Jan 17. Panorama No. 2018-25413447.

[c] Straka, M. Proprietary Name Review for Terlivaz (NDA 022231). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 APR 23. Panorama No. 2020-38454674.

- Route of Administration: Intravenous
- Dosage Form: for injection
- Strength: 0.85 mg per vial (equivalent to 1 mg of terlipressin acetate)
- Dose and Frequency:
    - Days 1-3: 1 mg every 6 hours
    - Day 4: Assess serum creatinine versus baseline
        - If serum creatinine (SCr) has decreased by at least 30% from baseline, continue 1 mg TERLIVAZ every 6 hours.
        - If SCr has decreased by less than 30% from baseline, dose may be increased to (b) (4) mg TERLIVAZ every 6 hours.
        - If SCr is at or above baseline value, discontinue Terlivaz.
    - Continue TERLIVAZ until 24 hours after two consecutive SCr ≤1.5 mg/dL values at least 2 hours apart or a maximum of 14 days.
- How Supplied: TERLIVAZ (terlipressin) is supplied as a sterile, preservative-free, lyophilized powder in single-dose vials containing (b) (4) 0.85 mg of terlipressin (b) (4) Each vial is supplied in a carton (NDC 43825-200-01).
- Storage: Store TERLIVAZ vials in the carton under refrigerated conditions at 2°C to 8°C (36°F to 46°F). Protect from light prior to reconstitution.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

[d] USAN stem search conducted on September 9, 2021.

2.2.2 Components of the Proposed Proprietary Name

Mallinckrodt indicated in their submission that the proposed proprietary name, Terlivaz, was derived from a combination of letters that is devoid of meaning. We note that the proposed proprietary name is composed of "Terli" which is the first part of the established name (terlipressin) and "vaz" which resembles the pharmacologic category (vasopressin analogue). However, from our postmarketing experience with approved drug products (e.g., Vasostrict, Pitressin, etc.), we do not anticipate any name confusion medication errors with this type of name composition. The proposed name is comprised of a single word that contains the letters 'iv', which is the abbreviation for the intravenous route of administration. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of this abbreviation in the middle of the name, and the lack of prominence of this abbreviation makes it unlikely that the letters 'iv' within the proposed proprietary name, Terlivaz, could lead to confusion in this case.

2.2.3 Comments from Other Review Disciplines at Initial Review

On September 3, 2021, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Terlivaz at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred and three (103) practitioners participated in DMEPA's prescription studies for Terlivaz.

In the computerized provider order entry (CPOE) study, one participant entered an incorrect sequence of letters, 't' instead of 'ter', when searching for the study name. After 170 seconds passed, the participant incorrectly selected the name 'Talicia', suggesting that the participant selected a random name in order to proceed with the simulation study. Thus, in this case, the study response is unlikely to be representative of a plausible CPOE based risk. We evaluate this name pair in Appendix E.

Additionally, in the computerized provider order entry (CPOE) study, when searching for the study name with the correct sequence of letters "ter", 2 participants incorrectly selected 'Terfenor' (n=1) and 'Terfonyl' (n=1). We evaluated the name pairs, Terlivaz vs. Terfenor and Terlivaz vs. Terfonyl, below:

Terlivaz vs. Terfenor:

Terfenor (terfenadine) is an international brandname formerly marketed in United Kingdom and South Africa. Terfenadine (previously marketed as Seldane in the US) has been withdrawn from markets worldwide due to risk of cardiac arrhythmia in the 1990s. Thus, the risk of name confusion between Terlivaz and Terfenor is minimized. We evaluate the name pair in Appendix G.

Terlivaz vs. Terfonyl:

Per Drugs@FDA, Terfonyl is discontinued with no generic equivalents available. NDA 006904 was withdrawn FR effective March 20, 2020. Thus, the risk of name confusion between Terlivaz and Terfonyl is minimized. We evaluate the name pair in Appendix G.

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

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[e] identified 162 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥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 6 names not previously analyzed. 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, prescription simulation study and (b) (4) 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 ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	6
Low similarity name pair: combined match percentage score ≤54%	6

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

Our analysis of the 12 names contained in Table 1 determined none of the names will pose a risk for confusion with Terlivaz as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA 2 communicated our findings to the Division of Cardiology and Nephrology (DCN). At that time we also requested additional information or concerns that could inform our review. On November 1, 2021, the Division of Cardiology and Nephrology (DCN) stated no additional concerns with the proposed proprietary name, Terlivaz.

[e] POCA search conducted on August 25, 2021 in version 4.4.

3 CONCLUSION

The proposed proprietary name, Terlivaz, is acceptable.

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

3.1 COMMENTS TO MALLINCKRODT PHARMACEUTICALS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on August 18, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

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

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

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

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

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

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, 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[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 likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

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

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

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

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

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

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

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

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

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

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

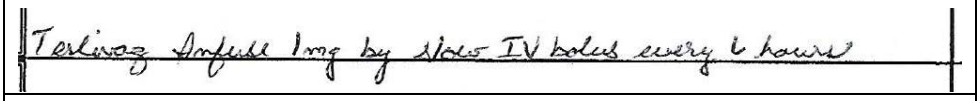
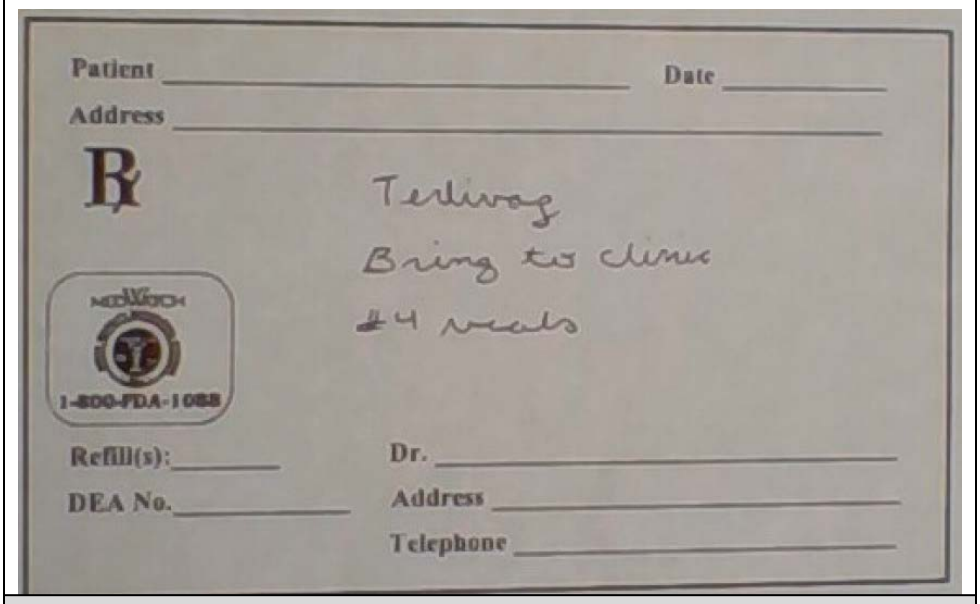
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Terlivaz Study (Conducted on August 27, 2021)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  Outpatient Prescription:  **CPOE Study Sample (displayed as sans-serif, 12-point, bold font)** Terlivaz	Terlivaz Bring to clinic #4 vials

FDA Prescription Simulation Responses (Aggregate Report)

260 People Received Study
103 People Responded

Study Name: Terlivaz

Total	30	26	23	24	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
TALICIA	0	1	0	0	1
TERFENOR	0	1	0	0	1
TERFONYL	0	1	0	0	1
TERIVAZ	0	0	0	1	1
TERLAVAZ	0	0	3	0	3
TERLEVAZ	0	0	1	0	1
TERLINAS	1	0	0	0	1
TERLIVAG	12	0	0	0	12
TERLIVAQ	3	0	0	1	4
TERLIVAZ	6	23	1	13	43
TERLIVAZ INFUSE	0	0	0	1	1
TERLIVOG	5	0	0	0	5
TERLIVOQ	2	0	0	0	2
TERLIVOZ	1	0	0	0	1
TERLOVAZ	0	0	1	0	1
TERLYVAZ	0	0	1	0	1
TERLIVAQ	0	0	0	1	1
TESLIVAZ	0	0	0	5	5
TESLIVAZ INFULL	0	0	0	1	1
TESLIVOZ	0	0	0	1	1
TIRLAVAZ	0	0	1	0	1
TIRLIVAZ	0	0	1	0	1
TRULAVAZ	0	0	1	0	1
TRULYVAZ	0	0	1	0	1
TURLAVAZ	0	0	8	0	8
TURLEVASZ	0	0	1	0	1
TURLEVAZ	0	0	1	0	1
TURLIVAZ	0	0	2	0	2

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

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.	(b) (4)***	56
2.	Travasol 8.5%	55

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:** Terlivaz **Established name:** terlipressin **Dosage form:** for injection **Strength(s):** 0.85 mg per vial (equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b) (4) mg every 6 hours in case of less than 30% decrease in serum creatinine from baseline.	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Norliqva***	62	This name pair has sufficient orthographic and phonetic differences.
2.	Talicia	53	Orthographically, the suffixes (vaz vs. cia) provides some orthographic differences. Phonetically, the third syllables (vaz vs. see) sound different. Terlivaz is comprised of three syllables whereas Talicia contains an extra fourth syllable (-ah). Although both Terlivaz and Talicia are both single strength products (0.85 mg/vial vs. 250 mg/10 mg/12.5 mg), this name pair differs in dosage form (for injection vs. fixed dose combination capsule), and route of administration (intravenous vs. fixed

No.	**Proposed name:** Terlivaz **Established name:** terlipressin **Dosage form:** for injection **Strength(s):** 0.85 mg per vial (equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b)(4) mg every 6 hours in case of less than 30% decrease in serum creatinine from baseline.	**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**
			dose combination capsule). Additionally, this name pair differs in recommended dose (1 mg to (b)(4) mg vs. 4 capsules), and frequency of administration (every 6 hours for a maximum of 14 days vs. every 8 hours for 14 days). Thus, the risk of name confusion between the pair is minimized.

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

No.	Name	POCA Score (%)
1.	Toviaz	54
2.	Tocilizumab	46
3.	Ceftazidime	36

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

No.	Name	POCA Score (%)	Failure preventions
1.	(b) (4) ***	62	Proposed proprietary name withdrawn by the Applicant on May 29, 2020 due to trademark issues. Subsequently, the Applicant submitted proposed proprietary name, Inmazeb, for evaluation. BLA 761169 was approved on October 14, 2020 under the proprietary name Inmazeb.
2.	Terfenor	52	Terfenor (terfenadine) is an international brandname formerly marketed in United Kingdom and South Africa. Terfenadine (previously marketed as Seldane in the US) has been withdrawn from markets worldwide due to risk of cardiac arrhythmia in the 1990s.
3.	Terfonyl	52	Per Drugs@FDA, Terfonyl is discontinued with no generic equivalents available. NDA 006904 was withdrawn FR effective March 20, 2020.

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

No.	Name	POCA Score (%)
1.	(b) (4) ***	60
2.	(b) (4) ***	60

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

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/s/

DEVIN R KANE
11/03/2021 11:08:38 AM

HINA S MEHTA
11/03/2021 12:39:01 PM

CHI-MING TU
11/03/2021 04:00:03 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:	April 23, 2020
Application Type and Number:	NDA 022231
Product Name and Strength:	Terlivaz (terlipressin) for Injection, 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Mallinckrodt Hospital Products IP Limited (Mallinckrodt)
Panorama #:	2020-38454674
DMEPA Safety Evaluator:	Maximilian Straka, PharmD, FISMP
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD, FISMP, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Terlivaz, 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. Mallinckrodt submitted an external name study, conducted by (b) (4) for this proposed proprietary name which was previously reviewed under IND 068582.

1.1 REGULATORY HISTORY

Many Applicants/Sponsors have been involved in the development of the proposed terlipressin for injection. DMEPA previously evaluated the proposed proprietary name, (b) (4) ***, (b) (4)

(b) (4)

Thus, the current Applicant Mallinckrodt submitted the name, Terlivaz, for review on March 12, 2020. We note that all product characteristics remain the same.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on March 12, 2020.

- Intended Pronunciation: TUR-lih-vaz
- Active Ingredient: terlipressin
- Indication of Use: Treatment of adults with hepatorenal syndrome (HRS) Type 1.
- Route of Administration: Intravenous
- Dosage Form: for Injection
- Strength: 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate)
- Dose and Frequency:
    - Days 1-3: 1 mg every 6 hours

(b) (4)

- Day 4: Assess serum creatinine versus baseline
    - If serum creatinine (SCr) has decreased by at least 30% from baseline, continue 1 mg TERLIVAZ every 6 hours.
    - If SCr has decreased by less than 30% from baseline, dose may be increased to (b) (4) mg TERLIVAZ every 6 hours.
    - If SCr is at or above baseline value, discontinue Terlivaz.
- Continue TERLIVAZ until 24 hours after two consecutive SCr ≤1.5 mg/dL values at least 2 hours apart or a maximum of 14 days.

- How Supplied: TERLIVAZ (terlipressin) is supplied as a sterile, preservative-free, lyophilized powder in single-dose vials containing (b) (4) 0.85 mg of terlipressin (b) (4) Each vial is supplied in a carton (NDC 43825-200-01).
- Storage: Store TERLIVAZ vials in the carton under refrigerated conditions at 2°C to 8°C (36°F to 46°F). Protect from light prior to reconstitution.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Mallinckrodt did not provide a derivation or intended meaning for the proposed proprietary name, Terlivaz, in their submission. We note that the proposed proprietary name is composed of "Terli" which is the first part of the established name (terlipressin) and "vaz" which resembles the pharmacologic category (vasopressin analogue). However, from our postmarketing experience with approved drug products (e.g., Vasostrict, Pitressin, etc.), we do not anticipate any name confusion medication errors with this type of name composition. The proposed name is comprised of a single word that contains the letters 'iv', which is the abbreviation for the intravenous route of administration. Although we typically discourage the inclusion of medical

[c] USAN stem search conducted on March 19, 2020.

abbreviations in proprietary names, we determined that the location of this abbreviation in the middle of the name, and the lack of prominence of this abbreviation makes it unlikely that the letters 'iv' within the proposed proprietary name, Terlivaz, could lead to confusion in this case.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 25, 2020 e-mail, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Terlivaz at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-two (92) practitioners participated in DMEPA's prescription studies for Terlivaz. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified 159 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥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 11 names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and (b) (4) 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 ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	9
Low similarity name pair: combined match percentage score ≤54%	0

[d] POCA search conducted on March 19, 2020 in version 4.3.

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

Our analysis of the 11 names contained in Table 1 determined none of the names will pose a risk for confusion with Terlivaz 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 Cardiology and Nephrology (DCN) via e-mail on April 21, 2020. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Cardiology and Nephrology (DCN) on April 23, 2020, they stated no additional concerns with the proposed proprietary name, Terlivaz.

3 CONCLUSION

The proposed proprietary name, Terlivaz, is acceptable.

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

3.1 COMMENTS TO MALLINCKRODT HOSPITAL PRODUCTS IP LIMITED

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

If any of the proposed product characteristics as stated in your submission, received on March 12, 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. [e]

[e] 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 ≥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[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.

   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 ≥ 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.

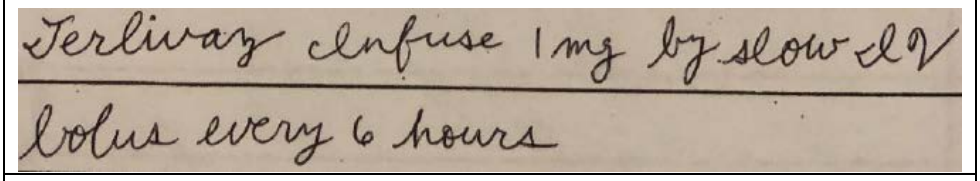
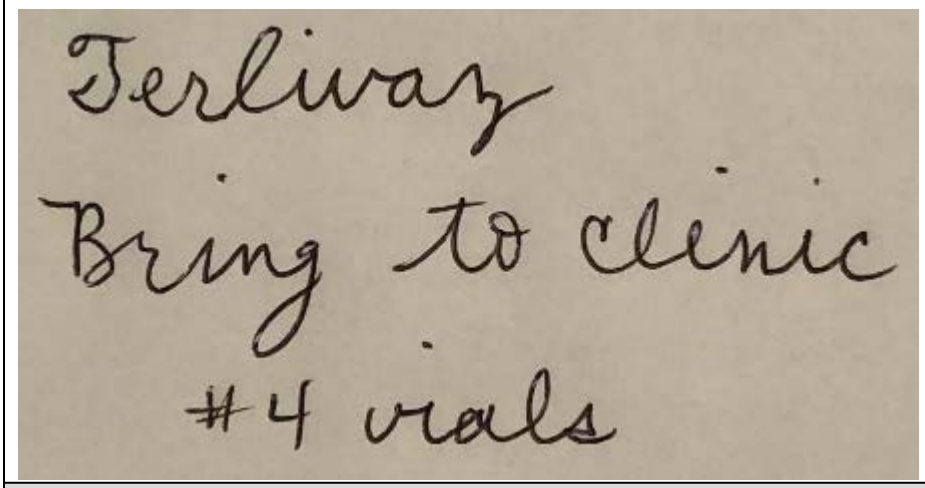
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Terlivaz Study (Conducted on March 24, 2020)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  Outpatient Prescription:  **CPOE Study Sample (displayed as sans-serif, 12-point, bold font)** Terlivaz	Terlivaz Bring to clinic Dispense # 4 Vials

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Terlivaz

As of Date 4/8/2020

209 People Received Study

92 People Responded

Study Name: Terlivaz

Total	34	18	16	24	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
JERLIVARZ	0	0	0	1	1
JERLIVAZ	2	0	0	1	3
JERLIVAZ INFUSE	0	0	0	1	1
PERLIVAZ	0	0	1	0	1
TERLABAS	0	0	1	0	1
TERLAVAZ	0	0	3	0	3
TERLIVAQ	1	0	0	0	1
TERLIVARY	1	0	0	0	1
TERLIVAY	0	0	0	2	2
TERLIVAZ	28	18	2	19	67
TERLIWAZ	1	0	0	0	1
TERLZVAR	1	0	0	0	1
TURLABAZE	0	0	1	0	1
TURLABYS	0	0	1	0	1
TURLAVAZ	0	0	4	0	4
TURLEVAZ	0	0	1	0	1
TURLIVAS	0	0	1	0	1
TURLOVAZ	0	0	1	0	1

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

No.	**Proposed name:** Terlivaz **Established name:** terlipressin **Dosage form:** for Injection **Strength(s):** 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b)(4) mg every six hours in case of less than 30% decrease in serum creatinine from baseline.	**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.	Terlivaz	100	This name is the subject of this review.
2.	Tetraviv	70	Orthographically, Terlivaz contains the upstroke letter "l" in the 4th position of the name vs. Tetraviv contains the cross-stroke letter "t" in the 3rd position of the name, providing some orthographic difference between the names. Additionally, when scripted with a downstroke "z", Terlivaz ends in a downstroke letter "z" that's not seen in Tetraviv. Phonetically, the second syllables (lih vs. tra) provide sufficient phonetic differences. Additionally, even though the third syllables (vaz vs. viv) begin with the same consonant, the "a" and "i" sounds in these syllables also makes the syllables sound different in this situation. Terlivaz*** and Tetraviv do not overlap in dose (1 mg to (b)(4) mg vs. thin coating) or strength (0.85 mg per vial vs. 2%). The products also differ in terms of dosage form (for injection vs. ointment), route of administration (intravenous vs. topical), and frequency of administration (every 6 hours vs. three times daily), which further

No.	**Proposed name:** Terlivaz **Established name:** terlipressin **Dosage form:** for Injection **Strength(s):** 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b) (4) mg every six hours in case of less than 30% decrease in serum creatinine from baseline.	**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.**
			minimizes the potential for an error to occur if included on a prescription.

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 (%)
	N/A	

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:** Terlivaz **Established name:** terlipressin **Dosage form:** for Injection **Strength(s):** 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b) (4) mg every six hours in case of less than 30% decrease in serum creatinine from baseline.	**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**
3.	(b) (4) ***	55	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Terlivaz **Established name:** terlipressin **Dosage form:** for Injection **Strength(s):** 0.85 mg per vial (0.85 mg of terlipressin free base equivalent to 1 mg of terlipressin acetate) **Usual Dose:** 1 mg by slow intravenous bolus every six hours for up to 14 days. The maximum daily dose may be increased to (b) (4) mg every six hours in case of less than 30% decrease in serum creatinine from baseline.	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
			(b) (4)
4.	Katerzia	56	This name pair has sufficient orthographic and phonetic differences.
5.	Tazverik	58	This name pair has sufficient orthographic and phonetic differences.
6.	(b) (4) ***	59	(b) (4)
7.	Trivisc	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 (%)
	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
8.	(b) (4) ***	60	Proposed proprietary name for IND 135058 found unacceptable by DMEPA (OSE# 2018-24459406). The proprietary name Orladeyo*** has been granted conditional approval under IND 135058 (OSE# 2018-26291674) and NDA 214094 (OSE# 2019-36180529).
9.	(b) (4) ***	55	CBER name found unacceptable 10/22/2018.
10.	(b) (4) ***	56	Proposed proprietary name for IND 125669 found unacceptable by DMEPA (OSE# 2019-28512596). The proprietary name Fyarro*** has been granted conditional approval under IND 125669 (OSE# 2019-34271077)

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 (%)
11.	(b) (4) ***	56

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

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	August 13, 2009
To:	Norman Stockbridge, M.D., Director Division of Cardiovascular and Renal Products
Through:	Melina Griffis, RPh, Acting Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Anne Crandall, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name:	Lucassin (Terlipressin Acetate) for Injection; 0.85 mg/vial
Application Type/Number:	NDA 22-231
Applicant:	Orphan Therapeutics, LLC
OSE RCM #:	2009-1128

*** **Note: This review contains proprietary and confidential information that should not be released to the public.** ***

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