CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214517Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	November 24, 2020
Application Type and Number:	NDA 214517
Product Name and Strength:	Hetlioz LQ (tasimelteon) oral suspension, 4 mg/mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Vanda Pharmaceuticals Inc. (Vanda)
Panorama #:	2020-42448497
DMEPA Safety Evaluator:	Loretta Holmes, BSN, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS
DMEPA Associate Director of Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Hetlioz LQ***, 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. Vanda did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Vanda currently markets Hetlioz (tasimelteon) capsules (NDA 205677), approved on January 31, 2014. It is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in adults.

Vanda resubmitted (after the Agency's previous Refuse-To-File action) supplement NDA 205677/S-007 for Hetlioz (tasimelteon) capsules and new NDA 214517 for Hetlioz oral suspension on June 1, 2020 for tasimelteon's use for the treatment of the sleep disorder in Smith-Magenis Syndrome (SMS). We note that the Prescribing Information for NDA 205667 and NDA 214517 will be shared.

On August 28, 2020, Vanda submitted the proposed name Hetlioz LQ*** under NDA 214517, for tasimelteon oral suspension.

1.2 PRODUCT INFORMATION

The following Hetlioz LQ*** and Hetlioz product information is provided in the proprietary name submission received on August 28, 2020 and draft updates to the Prescribing Information by the Division (see Table 1, below).

Table 1. Relevant Product Information for Hetlioz LQ and Hetlioz (shared Prescribing Information)

Product Name	**Hetlioz LQ*** **	**Hetlioz**
Initial Approval Date	N/A	January 31, 2014
Intended Pronunciation	het - li: - əʊz - ɛl - kju	het - li: - əʊz
Active Ingredient	tasimelteon	
Indication	Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)	Non-24-Hour Sleep-Wake Disorder (Non-24) Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)
Route of Administration	Oral	
Dosage Form	Oral suspension	Capsules
Strength	4 mg/mL	20 mg
Dose and Frequency	**Non-24-Hour Sleep-Wake Disorder (Non-24)** Adults (Capsules) The recommended dosage of is 20 mg one hour before bedtime, at the same time every night.	

<table>
<tr><td></td><td colspan="2">Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS)
<u>Patients 16 years and older (Capsules)</u>
The recommended dosage in adults is 20 mg one hour before bedtime, at the same time every night.
<u>Pediatric Patients 3 years to 15 years of age (Oral Suspension)</u>
The recommended dosage in pediatric patients is based on body weight (see Table 1). Administer one hour before bedtime, at the same time every night.
Table 1: Recommended Dosage for the Treatment of Nighttime Sleep Disturbances in Smith-Magenis Syndrome (SMS) in Pediatric Patients 3 Years to 15 Years of Age
<table>
<tr><th><u>Body Weight</u></th><th><u>Daily Dose (oral suspension)</u></th></tr>
<tr><td>≤ 28 kg</td><td>0.7 mg/kg one hour before bedtime</td></tr>
<tr><td>>28 kg</td><td>20 mg one hour before bedtime</td></tr>
</table></td></tr>
<tr><td>How Supplied</td><td>Carton containing: Bottle of oral suspension containing 48 mL or 158 mL, a press-in bottle adapter, and a 5 mL oral dosing syringe</td><td>Bottles of 30 capsules</td></tr>
<tr><td>Storage</td><td>Store oral suspension at refrigerated temperature 5°C (41°F); excursions permitted to 2°C to 8°C (36°F t o 46°F). (b) (4)</td><td>Store at controlled room temperature, 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]. Protect from exposure to light and moisture.</td></tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Hetlioz LQ*** would not misbrand the proposed product. OPDP noted that "Vanatol LQ" is a currently marketed product and deferred to DMEPA to assess the appropriateness of the inclusion of the modifier "LQ". The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Psychiatry (DP) concurred with the findings of OPDP's assessment for Hetlioz LQ***.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Hetlioz LQ***.

2.2.1 United States Adopted Names (USAN) Search

The proposed proprietary name, Hetlioz LQ***, contains the United States Adopted Name (USAN) stem "-io-" in the infix position of the name. The USAN stem "-io-" is used by the

USAN Council to indicate iodine-containing contrast media products products.[a] Proprietary names should not incorporate USAN stems in the position that USAN designates for the stem.[b] The use of a USAN stem within proprietary names, even when used consistently with the USAN meaning, can result in multiple similar proprietary names and proprietary names that are similar to established names, thus increasing the chance of confusion among those drugs, which may compromise patient safety. To reduce the potential for confusion, USAN stems should usually not be incorporated into proprietary names.

However, we determined that the two-letter stem "-io-" is often not distinct enough to be recognized as a USAN stem. We also note that the USAN Council has allowed the use of the stem "-io-" in established names (e.g., vortioxetine) as well as in other USAN stems (-tioxetine). This has resulted in conflicting stems, and therefore in those instances, the stem does not support the USAN Council naming convention or accurately indicate the pharmacological or chemical trait of the drug. Additionally, based on our postmarketing experience, we do not have the same safety concerns with the two-letter stems, including "-io-", that we have identified with USAN stems containing three or more letters.[c,d]

Furthermore, the root name, Hetlioz, is currently marketed and there is no postmarketing evidence that the stem has been a source of confusion in the name. Therefore, we do not object to the inclusion of the two-letter USAN stem "-io-" incorporated into the proposed proprietary name Hetlioz LQ.

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name is comprised of two components: 1) the root name, Hetlioz, and 2) the modifier, LQ. Vanda indicated the following in their proprietary name submission:

Tasimelteon (20 mg capsules) is currently approved under the proprietary name Hetlioz. The proprietary name Hetlioz stems from the desire to achieve a unique name with Greek/Latin roots for daylight/sunlight and is derived from "Helios," a Greek god of the sun. The proposed proprietary name Hetlioz LQ for tasimelteon (4 mg/mL suspension) is derived from the proprietary name currently in use for tasimelteon (20 mg capsules), "Hetlioz", and the suffix "LQ" meaning liquid. The use of the root name, Hetlioz, and the modifier, LQ, are evaluated in Section 2.2.5.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 29, 2020 e-mail, the Division of Psychiatry (DP) did not forward any comments or concerns relating to Hetlioz LQ*** at the initial phase of the review.

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[a] USAN stem search conducted on November 2, 2020.

[b] Guidance for industry: Best practices in developing proprietary names for drugs. Draft Guidance May 2014. http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM39899

[c] Institute for Safe Medication Practices. Safety briefs: Aripiprazole or rabeprazole? ISMP Med Saf Alert Acute Care. 2003;8(8):1-3.

[d] Institute for Safe Medication Practices. Safety Briefs. ISMP Med Saf Alert Acute Care. 2002;7(17):1-2.

2.2.4 FDA Name Simulation Studies

Eighty-four (84) practitioners participated in DMEPA's prescription studies for Hetlioz LQ***. Seventeen (17) participants interpreted the name as "Hetlioz" or a variant spelling and omitted the modifier "LQ". Additionally, eight participants in the inpatient study interpreted the modifier as "L2" and two participants in the inpatient study omitted the letter "Q" from the modifier. See Section 2.2.5 for our discussion on the impact of omitting the modifier from the proposed proprietary name, interpreting the modifier as "L2", or omitting the letter "Q" from the modifier. Appendix B contains the results from the prescription simulation studies.

2.2.5 Safety Assessment of the Proposed Name Hetlioz LQ

In this section, we provide a safety analysis of the proposed proprietary name Hetlioz LQ***. Vanda currently markets the active ingredient tasimelteon under the name Hetlioz (tasimelteon) for the capsule formulation. For their proposed tasimelteon oral suspension, Vanda proposes to use Hetlioz as the root name, with the addition of a modifier. As such, we evaluated the following: (1) use of the same root name, (2) use of a modifier to distinguish the products, and (3) the proposed modifier "LQ".

1. <u>Evaluation of the use of the same root name "Hetlioz"</u>

Hetlioz has been marketed as the proprietary name for tasimelteon since approval on January 31, 2014. We note that Hetlioz and Hetlioz LQ*** share the same active ingredient and have an overlapping indication of use. Our postmarketing surveillance has not identified any medication errors attributed to name confusion involving Hetlioz. Thus, we do not object to the use of the root name, Hetlioz, for this product.

2. <u>Evaluation of the use of a modifier to differentiate the products</u>

Vanda proposes to differentiate the proposed product, Hetlioz LQ***, from the currently marketed capsule formulation, Hetlioz, by using the modifier "LQ" in the proposed proprietary name nomenclature. Hetlioz LQ*** is an oral suspension and the use of a modifier may help to distinguish it from Hetlioz. It is not uncommon to use modifiers to denote a specific product formulation as part of a product line extension. We note that Hetlioz capsules are currently indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in adults. Vanda submitted an NDA supplement that proposes the use of Hetlioz capsules for treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients 16 years and older. However, the capsule formulation is not indicated for SMS in pediatric patients aged 3 years to 15 years; rather the proposed Hetlioz LQ*** oral suspension is indicated for SMS in this patient population (see Table 1 in Section 1.2, above). The addition of a modifier to the root name Hetlioz may help to differentiate the proposed oral suspension from the currently marketed capsules.

In our evaluation, we considered the risk of name confusion if the modifier is dropped. We note that omission and oversight of a modifier is cited in literature as a common cause of medication errors.[e] Postmarketing experience shows that the introduction of product line

[e] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

extensions may result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. We note that Hetlioz and Hetlioz LQ*** will have an overlapping dose (20 mg) for the SMS indication[f] and, thus, there is a potential for the administration of the wrong dosage form if the modifier is dropped. We note that the concern primarily lies with the risk of confusion between the 20 mg capsule dose for adults with Non-24-Hour Sleep-Wake Disorder (Non-24) or SMS patients aged 16 years and older and the 20 mg oral suspension dose for SMS patients aged 3 years to 15 years of age weighing more than 28 kg. Doses for SMS patients aged 3 years to 15 years of age weighing equal to or less than 28 kg are based on weight and not achievable through the available capsule strength.

According to the medical officer, "*the two formulations are not interchangeable. The safety of tasimelteon is benign, however we have very limited pediatric data and because the suspension is only indicated in children, the dosage scheme in the label should be followed strictly.*" Furthermore, we sent an information request to the Applicant on November 6, 2020 inquiring about the clinical consequences, safety concerns, and impact on efficacy if a patient received the Hetlioz capsules instead of the Hetlioz LQ oral suspension and vice versa. The Applicant stated that "*in the event that a prescriber inadvertently prescribes Hetlioz 20 mg capsules instead of Hetlioz 20 mg LQ, we do not foresee any clinical consequences, safety concerns, or impacts on efficacy since apparent clearance and exposure of Hetlioz and Hetlioz LQ at the 20 mg dose are similar (full response is available in docuBridge[g])*". We shared the Applicant's response with the medical officer and based on their review of the response, the medical officer further clarified that "*there is no safety issue if the two formulations are exchanged provided that the subjects take the recommended dosage. However, if you foresee the possibility that a 20 mg capsule is prescribed to a child below 28 kg…we only have data for the 20 mg dose or weight-based equivalent*".

Although we acknowledge that modifiers may be omitted or overlooked; when used, they can assist in differentiating products and may help to prevent potential product selection errors. Additionally, Hetlioz LQ*** is an oral suspension and additional differences in product characteristic information [e.g., strength (4 mg/mL), dosage form (suspension), and dose (if less than 20 mg)] when written on a prescription, may provide an added measure of safety.

An alternative to using a modifier to distinguish this proposed product from the currently marketed product is to use a different proprietary name (i.e., one that does not use the root name Hetlioz). However, marketing the new product under a unique proprietary name also carries a risk of medication errors, including the potential for patients to be inadvertently placed on multiple tasimelteon products (therapeutic duplication) if the proprietary names are not recognized as having the same active ingredient. This may lead to overdose and adverse drug events. These errors may have greater associated safety risks than the omission or oversight of the modifier as discussed above. Thus, based on the totality of this information, we do not object to the use of a modifier for this product.

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[f] Patients aged 16 years and older: 20 mg capsule one hour before bedtime; Pediatric patients aged 3 years to 15 years of age weighing more than 28 kg: 20 mg oral suspension (or 5 mL) one hour before bedtime.

[g] Re: NDA 214517-Response to Proprietary Name Review Information Request received November 6, 2020.Vanda Pharmaceuticals Inc., Nov 10, 2020, available at: \\CDSESUB1\evsprod\nda214517\0033\m1\us\118-prop-names\resp-prop-names-20201106.pdf

3. Evaluation of the proposed modifier "LQ"

According to Vanda, the intended meaning of the modifier "LQ" is "liquid". However, Vanda did not provide any data in support of the use of the modifier. We note that the name Serostim LQ is on the Institute of Safe Medication Practices' (ISMP) List of Products with Drug Name Suffixes[h] and the meaning provided is "liquid". Additionally, we note that the following previously or currently marketed products have the "LQ" modifier: Entex LQ, Nohist LQ, Vanatol LQ, Vtol LQ, Lortuss LQ, and Miclara LQ. These are oral liquid over-the-counter products or prescription products; however, the proprietary names were not reviewed by DMEPA. Additionally, we note that we have not identified any postmarketing cases of name confusion associated with the modifier 'LQ'. We also note that the modifier is not misleading since its intended meaning is "liquid" and Hetlioz LQ*** is a liquid. Furthermore, if the modifier was misinterpreted as "SQ" or subcutaneous, for instance, it is unlikely that the product would be given subcutaneously because it is an oral suspension and its dosing, labeling, and packaging (press in bottle adaptor, oral dosing syringe) do not support a subcutaneous route of administration.

We acknowledge that eight participants in the inpatient study interpreted the modifier as "L2"; however, we note that the writing sample was poorly written. Two participants in the inpatient study omitted the letter "Q" from the modifier (i.e., interpreted the name as Hetlioz L); however, we do not have concerns that this misinterpretation would lead to a medication error.

Thus, considering the totality of information, we do not object to the use of the modifier "LQ" for this product.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Psychiatry (DP) via e-mail on November 24, 2020.

3 CONCLUSION

The proposed proprietary name, Hetlioz LQ***, is acceptable.

If you have any questions or need clarifications, please contact Phuong B. Nguyen, OSE Project Manager, at 240-402-5827

3.1 COMMENTS TO VANDA PHARMACEUTICALS INC.

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

[h] ISMP's List of Products with Drug Name Suffixes [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2010. Available from: https://www.ismp.org/sites/default/files/attachments/2018-04/drugnamesuffixes.pdf

If any of the proposed product characteristics as stated in your submission, received on August 28, 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.

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. [i]

***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)).

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

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[j]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
- 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.

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,

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

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	**Y/N**	Do the syllables have different phonologic processes, such

	a different number or placement of upstroke/downstroke letters present in the names?		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.

<table>
<tr><td></td><td colspan="2">• Similar sounding doses: 15 mg is similar in sound to 50 mg</td></tr>
<tr><td rowspan="2">Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</td></tr>
<tr><td>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?</td><td>Phonetic Checklist (Y/N to each question)
• Do the names have different number of syllables?
• Do the names have different syllabic stresses?
• Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
• Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

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. Hetlioz LQ* Study (Conducted on September 15, 2020)**

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: Hetlioz LQ 20 mg po once daily, one hour before bedtime	Hetlioz LQ Take 5 mL orally once daily, one hour before bedtime Dispense (b) (4) mL bottle
Outpatient Prescription: Hetlioz LQ Take 5mL orally once daily, one hour before bedtime Dispense (b) (4) mL bottle	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Hetlioz LQ	

FDA Prescription Simulation Responses (Aggregate Report)

				208 People Received Study	
				84 People Responded	
Study Name: Hetlioz LQ					
Total	**17**	**29**	**20**	**18**	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
`HETLIOZ LQ	1	0	0	0	1
HADLIOS	0	0	1	0	1
HEADLEO LQ	0	0	1	0	1
HEADLIOS LQ	0	0	1	0	1

HECLIOUS LQ	0	0	1	0	1
HEDLIOS LQ	0	0	4	0	4
HEDLIOSE LQ	0	0	1	0	1
HEDLIOSS LQ	0	0	1	0	1
HELPLIOS LQ	0	0	1	0	1
HEPLIOS	0	0	1	0	1
HEPLIOS LQ	0	0	3	0	3
HETLIOS LQ	0	0	2	0	2
HETLIOSE LQ	0	0	1	0	1
HETLIOZ	0	7	0	8	15
HETLIOZ L	0	0	0	2	2
HETLIOZ L2	0	0	0	8	8
HETLIOZ LQ	16	22	0	0	38
PEDLIOS LQ	0	0	1	0	1
TESLIO LQ	0	0	1	0	1

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/

LORETTA HOLMES
11/24/2020 02:59:23 PM

SEVAN H KOLEJIAN
11/24/2020 03:46:19 PM

MISHALE P MISTRY
11/24/2020 03:48:01 PM