

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761225Orig1s000

PROPRIETARY NAME REVIEW(S)

SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	12/5/2023
Responsible OND Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761225
Product Name and Strength:	Letybo (letibotulinumtoxinA-wlbq) for injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Hugel, Inc. (Hugel)
Nexus NPNS ID #:	2023-204
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

1 PURPOSE OF REVIEW

This review is to reassess the FDA-generated suffix, -wlbq, for BLA 761225, which was found conditionally acceptable on December 27, 2021^a and January 20, 2023^b for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761225.

1.1 Regulatory History

- FDA generated a four-letter suffix, -wlbq, for BLA 761225 on December 27, 2021^a.
- BLA 761225 received a Complete Response (CR) letter on March 31, 2022^c.
- Hugel submitted a Class 2 Resubmission on October 6, 2022.
- We found the suffix -wlbq, conditionally acceptable upon re-review on January 20, 2023^d.
- BLA 761225 received a Complete Response (CR) letter on April 12, 2023^e.
- Hugel submitted a Class 2 Resubmission on August 31, 2023.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the previously generated four-letter suffix, -wlbq, using the principles described in the applicable guidance^f.

We determined that the FDA-generated suffix -wlbq, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be

^a Mena-Grillasca, C. Nonproprietary Name Suffix Review for letibotulinumtoxinA-wlbq (BLA 761225). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Dec 27. Nexus NPNS ID No.: 2021-20.

^b Mena-Grillasca, C. Nonproprietary Name Suffix Review for letibotulinumtoxinA-wlbq (BLA 761225). Silver Spring (MD): FDA, CDER, OSE, OMEPRM, DMEPA 1 (US); 2023 Jan 20. Nexus NPNS ID No. 2022-137.

^c Beitz, JG. Complete Response (BLA 761225). Silver Spring (MD): FDA, CDER, OND, OII (US); 2022 Mar 31.

^d Mena-Grillasca, C. Nonproprietary Name Suffix Review for letibotulinumtoxinA-wlbq (BLA 761225). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Dec 27. Nexus NPNS ID No.: 2022-173.

^e Beitz, JG. Complete Response (BLA 761225). Silver Spring (MD): FDA, CDER, OND, OII (US); 2023 Apr 12.

^f Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA 1 ANALYSIS

These findings were shared with OPDP. On November 22, 2023, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 1 also communicated our findings to the Division of Dermatology and Dentistry (DDD) on December 5, 2023.

4 CONCLUSION

We find the suffix -wlbq acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to letibotulinumtoxinA-wlbq.

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/s/

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PROPRIETARY NAME MEMORANDUM

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	October 16, 2023
Application Type and Number:	Application Type Number/S-000
Product Name and Strength:	Letybo (established name) ^a for injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Choose an item
Applicant/Sponsor Name:	Hugel, Inc (Hugel)
PNR ID #:	2023-1044725329
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Acting Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

^a The nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as “letibotulinumtoxinA -xxxx” throughout this review in place of the nonproprietary name for this product.

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Letybo, which was found conditionally acceptable under BLA 761225 on December 27, 2022.^b On April 12, 2023, BLA 761225 was issued a complete response (CR) action. Thus, Hugel submitted the name, Letybo, under BLA 761225 for review on August 31, 2023 as part of their CR resubmission. 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 Letybo would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Letybo. The Division of Dermatology and Dentistry (DDD) concurred with the findings of OPDP's assessment for Letybo.

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 September 8, 2023 search of USAN stems did not find any USAN stems in the proposed proprietary name, Letybo.

2.3 COMMUNICATION OF DMEPA'S DETERMINATION

On October 16, 2023, we communicated our determination to the Division of Dermatology and Dentistry (DDD).

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, Letybo, is conditionally acceptable.

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

^b Howard, C. Proprietary Name Review for Letybo (BLA 761225). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 Dec 27. PNR ID No. 2022-1044724792.

3.1 COMMENTS TO HUGEL, INC

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

If any of the proposed product characteristics as stated in your submission, received on August 31, 2023, 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.

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/s/

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SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	1/20/2023
Responsible OND Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761225
Product Name and Strength:	Letybo (letibotulinumtoxinA-wlbq) for injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Hugel, Inc. (Hugel)
Nexus NPNS ID #:	2022-137
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 1 Director (acting):	Irene Z Chan, PharmD, BCPS

1 PURPOSE OF REVIEW

This review is to reassess the FDA-generated suffix, -wlbq, for BLA 761225, which was found conditionally acceptable on December 27, 2021^a, for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761225.

1.1 Regulatory History

FDA generated a four-letter suffix, -wlbq, for BLA 761225 on December 27, 2021^a. However, BLA 761225 received a Complete Response (CR) letter on March 31, 2022^b. Thus, Hugel submitted a Class 2 Resubmission on October 6, 2022.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the previously generated four-letter suffix, -wlbq, using the principles described in the applicable guidance^c.

We determined that the FDA-generated suffix -wlbq, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA 1 ANALYSIS

These findings were shared with OPDP. On January 17, 2023, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 1 also communicated our findings to the Division of Dermatology and Dentistry (DDD) on January 20, 2023.

^a Mena-Grillasca, C. Nonproprietary Name Suffix Review for letibotulinumtoxinA-wlbq (BLA 761225). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Dec 27. Nexus NPNS ID No.: 2021-20.

^b Beitz, JG. Complete Response (BLA 761225). Silver Spring (MD): FDA, CDER, OND, OII (US); 2022 Mar 31.

^c Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

4 CONCLUSION

We find the suffix -wlbq acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to letibotulinumtoxinA-wlbq. DMEPA 1 will communicate our findings to the Applicant via letter.

4.1 Recommendation for Hugel, Inc.

We find the nonproprietary name, letibotulinumtoxinA-wlbq, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, letibotulinumtoxinA-wlbq will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review. However, please be advised that if your application receives a complete response, the acceptability of this suffix will be re-evaluated when you respond to the deficiencies. If we find the suffix unacceptable upon our re-evaluation, we will inform you of our findings.

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/s/

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IRENE Z CHAN
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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	December 27, 2022
Application Type and Number:	BLA 761225
Product Name and Strength:	Letybo (letibotulinumtoxinA-xxxx) ^a for injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Hugel, Inc. (Hugel)
PNR ID #:	2022-1044724792
DMEPA 1 Safety Evaluator:	Corwin D. Howard, PharmD, RPh
Acting DMEPA 1 Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

^aThe nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as “letibotulinumtoxinA -xxxx” throughout this review in place of the nonproprietary name for this product.

Contents

1	INTRODUCTION	1
1.1	Regulatory History	1
1.2	Product Information	1
2	RESULTS.....	1
2.1	Misbranding Assessment	2
2.2	Safety Assessment.....	2
3	CONCLUSION	3
3.1	Comments to the Applicant/Sponsor	4
4	REFERENCES	5
	APPENDICES	6

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Croma Pharma GmbH and Hugel previously submitted the proposed proprietary name, Letybo*** under IND 123178 on January 29, 2021, and under BLA 761225 on March 31, 2021, respectively, which was found conditionally acceptable.^b However, BLA 761205 received a Complete Response (CR) on March 31, 2022.

Thus, Hugel responded to the CR and re-submitted the name, Letybo, for review under BLA 761225 on October 6, 2022.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on October 6, 2022.

- Intended Pronunciation: le ty'e boe
- Nonproprietary Name: letibotulinumtoxinA-xxxx
- Indication of Use: temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and/or corrugator muscle activity in adults
- Route of Administration: intramuscular
- Dosage Form: for injection
- Strength: 50 units/vial and 100 units/vial
- Dose and Frequency: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment. Single dose. No more frequently than every 3 months
- How Supplied: freeze-dried powder supplied in a single-dose vial with 50 units or 100 units
- Storage: stored in a refrigerator between 2° to 8°C (36° to 46° F), protect from light

2 RESULTS

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

^b Patel, M. Proprietary Name Review for Letybo (IND 123178 and BLA 761225). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 JUN 14. PNR ID No. 2021-1044723786 (IND) and 2021-1044723898 (BLA 761225).

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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

Hugel did not provide a derivation or intended meaning for the proposed proprietary name, Letybo, in their submission. We note that the proposed name, Letybo, is composed almost entirely of letters that are common to the nonproprietary name, “letibotulinumtoxinA-xxxx”. However, since the proposed product contains letibotulinumtoxinA-xxxx, and does not make reference to any inactive ingredients, we could not identify a plausible medication error risk related to the proprietary name referencing the proper name. Thus, we do not find the inclusion of the letters of the proper name in the proprietary name to be inaccurate or misleading. This proprietary name is comprised of a single word. We note that the proposed proprietary name contains the medical abbreviation “LE” (abbreviation for lower extremity; lupus erythematosus). Although we typically discourage the inclusion of medical abbreviations in the proprietary names, we determined that based on placement of the abbreviation as well as the context of use, these are unlikely to be misinterpreted in a manner that could lead to a medication error in this case. Thus, in this particular case, we find the inclusion of this medical abbreviation acceptable. Beyond these noted abbreviations, we note that Letybo does not contain any additional components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On October 28, 2022, the Division of Dermatology and Dentistry (DDD) did not forward any comments or concerns relating to Letybo at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-one (91) practitioners participated in DMEPA’s prescription studies for Letybo. 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.

^c USAN stem search conducted on November 18, 2022.

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

Our POCA search^d identified 40 names with the combined score of $\geq 55\%$ or individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 3 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. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	3
Low similarity name pair: combined match percentage score $\leq 54\%$	0

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

Our analysis of the 4 names contained in Table 1 determined none of the names will pose a risk for confusion with Letybo as described in Appendices C through H.

2.2.8 *Communication of DMEPA's Determination*

On December 27, 2022, DMEPA 1 communicated our determination to the Division of Dermatology and Dentistry (DDD).

3 CONCLUSION

The proposed proprietary name, Letybo, is conditionally acceptable.

If you have any questions or need clarifications, please contact Tri Bui-Nguyen, OSE project manager, at 240-402-3726.

^d POCA search conducted on November 18, 2022 in version 5.0.

3.1 COMMENTS TO HUGEL, INC.

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

If any of the proposed product characteristics as stated in your submission, received on October 6, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. **Phonetic and Orthographic Computer Analysis (POCA)**

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

Drugs@FDA

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

RxNorm

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

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

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm

(<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html>).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.^e

^e National Coordinating Council for Medication Error Reporting and Prevention. <https://www.nccmerp.org/about-medication-errors> Last accessed 10/05/2020.

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

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

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.

- Low similarity: combined match percentage score $\leq 54\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names^f. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
 - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

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

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

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

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

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

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

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

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

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

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

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

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

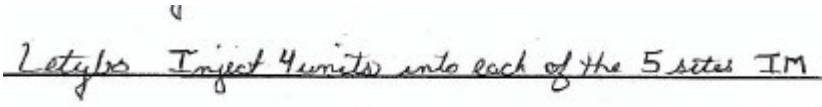
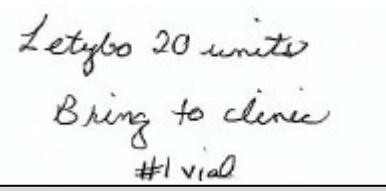
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. - Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names? - Is there different number or placement of cross-stroke or dotted letters present in the names? - Do the infixes of the name appear dissimilar when scripted? - Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) - Do the names have different number of syllables? - Do the names have different syllabic stresses? - Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? - Across a range of dialects, are the names consistently pronounced differently?
--	--	---

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Letybo Study (Conducted on October 31, 2022)

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

FDA Prescription Simulation Responses (Aggregate Report)

264 People Received Study

91 People Responded

Study Name: Letybo

Total	26	22	20	23	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
LATIBO	0	0	2	0	2
LATIBO 20 UNITS	0	0	1	0	1
LATIVO	0	0	1	0	1
LATYBO	0	0	2	0	2
LEDYBO	0	0	1	0	1
LEKTAIBO	0	0	1	0	1
LETIBO	0	0	2	0	2
LETTYBO	1	0	0	0	1
LETUBO	0	0	0	1	1
LETYBO	21	22	2	22	67
LETYBO INJECTION	1	0	0	0	1
LETYVO	0	0	4	0	4
LITIBO	0	0	1	0	1
LITIEBO	0	0	1	0	1
LITIVO	0	0	1	0	1
LITYBO	0	0	1	0	1
ZETYBO	3	0	0	0	3

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

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose – N/A

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

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment.	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.	Lytgobi	60	This name pair has sufficient orthographic and phonetic differences. Although Letybo and Lytgobi can share numerical similarity in dose (20 units vs. 20 mg), the recommended dose of Letybo*** is 4 unit (vs. the total dose of 20 units per treatment). Additionally, the name pair differs in strength (50 units/vial and 100 units/vial vs. 4 mg), dosage form (for injection vs. tablets), route of administration (intramuscular into each of the 5 sites vs. oral), and frequency of administration (no more frequently than every 3 months vs. once daily).
2.	^{(b) (4)} ***	58	This name pair has sufficient orthographic and phonetic differences.
3.	Leqembi***	56	Orthographically, the infixes (ty vs. qem) and last letters (o vs. i) provide sufficient orthographic differences.

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment.	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
			Phonetically, the second syllables (tye' vs. kem') and the ending sounds of the third syllables (boe vs. bee) sound different when spoken. Additionally, there is no overlap in dose [4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle); total dose of 20 units (0.5 mL) per treatment vs. 10 mg/kg/dose]. If route of administration (intramuscular vs. intravenous) is included on the medication order/prescription, there is no overlap between the products.

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

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

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

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

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CORWIN D HOWARD
12/27/2022 09:41:31 AM

MADHURI R PATEL
12/27/2022 10:24:34 AM

MISHALE P MISTRY
12/28/2022 09:37:23 AM

SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	12/27/2021
Responsible OND Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761225
Product Name and Strength:	Letybo (letibotulinumtoxinA-wlbq) for injection, 50 Units/vial and 100 Units/vial
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Hugel, Inc. (Hugel)
Nexus NPNS ID #:	2021-20
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 1 Director:	Irene Z. Chan, PharmD, BCPS

1 PURPOSE OF REVIEW

This review summarizes our evaluation of the four-letter suffix for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761225.

1.1 Regulatory History

Hugel was notified of the Agency's intention to designate a nonproprietary name that includes a four-letter distinguishing suffix that is devoid of meaning for their product in an Advice Letter^a.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

letibotulinumtoxinA-wlbg

FDA generated a four-letter suffix, -wlbg. This suffix was evaluated using the principles described in the applicable guidance^b.

We determined that the FDA-generated suffix -wlbg, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA 1 ANALYSIS

These findings were shared with OPDP. On December 21, 2021, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 1 also communicated our findings to the Division of Dermatology and Dentistry (DDD) on December 27, 2021.

^a Harris, D. General Advice Letter for BLA 761225. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US) 2021 Apr 19.

^b See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry:

Nonproprietary Naming of Biological Products. 2017. Available from:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

4 CONCLUSION

We find the suffix -wlbq acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to letibotulinumtoxinA-wlbq. DMEPA 1 will communicate our findings to the Applicant via letter.

4.1 Recommendation for Hugel, Inc.

We find the nonproprietary name, letibotulinumtoxinA-wlbq, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, letibotulinumtoxinA-wlbq will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review. However, please be advised that if your application receives a complete response, the acceptability of this suffix will be re-evaluated when you respond to the deficiencies. If we find the suffix unacceptable upon our re-evaluation, we will inform you of our findings.

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/

CARLOS M MENA-GRILLASCA
12/27/2021 09:39:37 AM

IRENE Z CHAN
12/30/2021 08:55:19 AM

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	June 14, 2021
Application Type and Number:	IND 123178 and BLA 761225
Product Name and Strength:	Letybo (letibotulinumtoxinA-xxxx) ^a for injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Croma-Pharma GmbH and Hugel, Inc. (Croma-Pharma and Hugel)
PNR ID #:	2021-1044723786 (IND 123178) 2021-1044723898 (BLA 761225)
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS
DMEPA Director (Acting)	Lubna Merchant, MS, PharmD

^a The proposed nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as “letibotulinumtoxinA-xxxx” throughout this review in place of the nonproprietary name for this product.

Contents

1	INTRODUCTION	1
1.1	Product Information.....	1
2	RESULTS.....	1
2.1	Misbranding Assessment	1
2.2	Safety Assessment	1
3	CONCLUSION	3
3.1	Comments to Croma-Pharma GmbH and Hugel, Inc.	3
	REFERENCES	4
	APPENDICES	5

1 INTRODUCTION

This review evaluates the proposed proprietary name, Letybo, 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. Croma-Pharma and Hugel did not submit an external name study for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on January 29, 2021 under IND 123178 and March 31, 2021 under BLA 761225.

- Intended Pronunciation: le ty'e boe
- Nonproprietary Name: letibotulinumtoxinA-xxxx
- Indication of Use: temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adults
- Route of Administration: intramuscular
- Dosage Form: for injection
- Strength: 50 units/vial and 100 units/vial
- Dose and Frequency: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator (b) (4) muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment
- Single dose. No more frequently than every 3 months
- How Supplied: freeze-dried powder supplied in a single-dose vial with 50 units or 100 units
- Storage: stored in a refrigerator between 2°C to 8°C (36°F to 46°F)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Croma-Pharma and Hugel did not provide a derivation or intended meaning for the proposed proprietary name, Letybo, in their submission. Croma-Pharma and Hugel stated the proprietary name is wholly fabricated name without reference to other products. We note that the proposed name, Letybo, is composed almost entirely of letters that are common to the nonproprietary name, “letibotulinumtoxinA-xxxx”. However, since the proposed product contains letibotulinumtoxinA-xxxx, and does not make reference to any inactive ingredients, we could not identify a plausible medication error risk related to the proprietary name referencing the proper name. Thus, we do not find the inclusion of the letters of the proper name in the proprietary name to be inaccurate or misleading. This proprietary name is comprised of a single word. We note that the proposed proprietary name contains the medical abbreviation “LE” (abbreviation for lower extremity; lupus erythematosus). Although we typically discourage the inclusion of medical abbreviations in the proprietary names, we determined that based on placement of the abbreviation as well as the context of use, these are unlikely to be misinterpreted in a manner that could lead to a medication error in this case. Thus, in this particular case, we find the inclusion of this medical abbreviation acceptable. Beyond these noted abbreviations, we note that Letybo does not contain any additional components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On March 16, 2021 and June 4, 2021, the Division of Dermatology and Dentistry (DDD) did not forward any comments or concerns relating to Letybo at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy (n=70) practitioners participated in DMEPA’s prescription studies for Letybo. 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^c identified 37 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score $\geq 70\%$. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

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

^b USAN stem search conducted on April 27, 2021.

^c POCA search conducted on April 27, 2021 in version 4.4.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	34
Low similarity name pair: combined match percentage score $\leq 54\%$	2

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

Our analysis of the 37 names contained in Table 1 determined none of the names will pose a risk for confusion with Letybo 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 Dermatology and Dentistry (DDD). At that time, we also requested additional information or concerns that could inform our review. On June 11, 2021, the Division of Dermatology and Dentistry (DDD) stated no additional concerns with the proposed proprietary name, Letybo.

3 CONCLUSION

The proposed proprietary name, Letybo, is acceptable.

If you have any questions or need clarifications, please contact Tri Minh Bui-Nguyen, OSE project manager, at 240-402-3726.

3.1 COMMENTS TO CROMA-PHARMA GMBH AND HUGEL, INC.

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

If any of the proposed product characteristics as stated in your submissions, received on January 29, 2021 and March 31, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. *Phonetic and Orthographic Computer Analysis (POCA)*

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.^d

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

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

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

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.

- Low similarity: combined match percentage score $\leq 54\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names^e. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
 - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

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

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

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

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

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

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

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

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

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

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

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

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

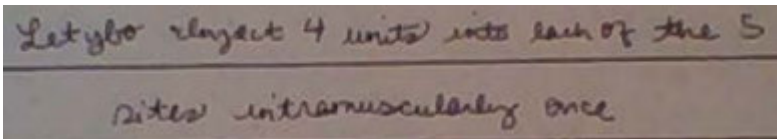
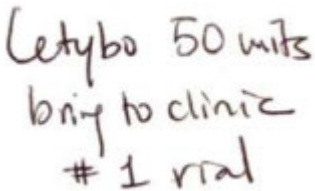
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Letybo Study (Conducted on March 23, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Letybo Bring to clinic. Dispense 1 vial.
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Letybo	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Letybo 209 People Received Study 70 People Responded					
Total	27	14	11	18	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
CETYBO	2	0	0	0	2
LATYBO	0	0	1	0	1
LAYTIBO	0	0	1	0	1
LETBO	1	0	0	0	1
LETIBO	0	0	2	0	2
LETYBO	23	14	2	16	55
LETYBO 50 UNITS	1	0	0	0	1

LETYBO INJECT	0	0	0	1	1
LETYBOLD	0	0	1	0	1
LEYBO	0	0	0	1	1
LITAIBO	0	0	2	0	2
LYTBIO	0	0	1	0	1
RETIVAL	0	0	1	0	1

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

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment	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.	Letybo***	100	Subject of this review.

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

No.	Name	POCA Score (%)
1.	(b) (4) ***	63

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

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment	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.	Lortab	60	This name pair has sufficient orthographic and phonetic differences.
2.	Lortab 10	60	This name pair has sufficient orthographic and phonetic differences.
3.	Libtayo	58	This name pair has sufficient orthographic and phonetic differences.

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment	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
4.	Leqvio***	56	Orthographically, the upstroke letter ‘t’ in the 3rd position for Letybo as compared to the downstroke letter ‘q’ in the 3rd position of Leqvio*** and the infixes/suffixes (‘ybo’ vs. ‘vio’) provides sufficient orthographic differences. Phonetically, the ending sounds of the first syllables (‘e’ vs. ‘q’), the second syllables (‘tye’ vs. ‘vee’), and the starting sounds of the third syllables (‘b’ vs. ‘o’) provides sufficient phonetic differences. Additionally, there is no overlap in strength [50 units/vial and 100 units/vial vs. 284 mg/1.5 mL (189 mg/mL)] and dose [4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator ^{(b) (4)} muscle and 1 injection in the procerus muscle); total dose of 20 units (0.5 mL) per treatment vs. 284 mg]. If route of administration (intramuscular vs. subcutaneous) is included on the medication order/prescription, there is no overlap between the products.
5.	Lessina	56	This name pair has sufficient orthographic and phonetic differences.
6.	Lessina-28	56	This name pair has sufficient orthographic and phonetic differences.

No.	Proposed name: Letybo Established name: letibotulinumtoxinA-xxxx Dosage form: for injection Strength(s): 50 units/vial and 100 units/vial Usual Dose: 4 units (0.1 mL) into each of 5 sites (2 injections in each corrugator muscle and 1 injection in the procerus muscle). A total dose of 20 units (0.5 mL) per treatment	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
7.	Lexette	56	This name pair has sufficient orthographic and phonetic differences.
8.	Tybost	56	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
1.	Latuda	54
2.	Ethyol	50

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.	Lortab 0.5/33.3	60	This name was identified in the RxNorm database and no product characteristics could be found using the commonly used databases.
2.	Lentizol	58	International product formerly marketed in Ireland and United Kingdom.
3.	Levatol	58	Name identified in RxNorm database and Drugs@FDA. Brand discontinued with no generic equivalents available.
4.	Bretylol	56	Brand discontinued with no generic equivalents available. NDA 017954 withdrawn FR effective 06/10/1999.
5.	Lente	56	Brand discontinued with no generic equivalent available. NDA 18383 was withdrawn FR effective 09/17/2003.

No.	Name	POCA Score (%)	Failure preventions
6.	Leptin	56	Product is not a drug. It is a hormone made by adipose cells that helps regulate energy balance by inhibiting hunger. It is also an ingredient in a homeopathic formulation, Slim.
7.	Lessina-21	56	Brand, Levlite-21 discontinued with no generic equivalents available. NDA 020860 withdrawn FR effective 04/18/2012.
8.	(b) (4) ***	56	Proposed proprietary name for IND 115333 found unacceptable by DMEPA (OSE# 2016-10674485). Subsequently, the proposed proprietary name Releuko*** was found conditionally acceptable for IND 115333 and BLA 761082.

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

No.	Name	POCA Score (%)
1.	Placebo	64
2.	Aler-Tab	58
3.	Booty Goo	58
4.	(b) (4) ***	58
5.	Ala Seb	56
6.	Ala-Tet	56
7.	Betimol	56
8.	(b) (4) ***	56
9.	Clostebol	56
10.	Elelyso	56
11.	Elyxyb	56
12.	Oleptro	56
13.	Platet	56
14.	Alu-Tab	55
15.	Cyltezo	55
16.	Okebo	55
17.	Rebetol	55

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

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/s/

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