CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761347Orig1s000

PROPRIETARY NAME REVIEW(S)

SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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Date of This Review:	6/28/2024
Responsible OND Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761347
Product Name and Strength:	Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs) injection 1,875 mg and 30,000 units per 15 mL (125 mg and 2,000 units per mL)
Product Type:	Multiple Ingredient Product
Applicant/Sponsor Name:	Genentech, Inc. (Genentech)
Nexus NPNS ID #:	2023-217
DMEPA 2 Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD

1 PURPOSE OF REVIEW

This review is to reassess the FDA-generated suffix, -tqjs, for BLA 761347, which was found conditionally acceptable on June 16, 2023[a], for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761347.

2 REGULATORY HISTORY

FDA-generated suffix, -tqjs, was found acceptable for BLA 761347 on June 16, 2023. However, Genentech requested to withdraw the application on August 31, 2023. Thus, Genentech resubmitted BLA 761347 on November 15, 2023.

3 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the previously generated four-letter suffix, -tqjs, using the principles described in the applicable guidance[b].

We determined that the FDA-generated suffix -tqjs, 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.

4 COMMUNICATION OF DMEPA 2 ANALYSIS

These findings were shared with OPDP. On June 26, 2024, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Oncology 2 (DO2) on June 28, 2024.

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[a] Mena-Grillasca, C. Nonproprietary Name Suffix Review for atezolizumab and hyaluronidase-tqjs (BLA 761347). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 Jun 16. Nexus No.: 2022-155.

[b] Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

5 CONCLUSION

We find the suffix -tqjs acceptable and recommend the nonproprietary name atezolizumab and hyaluronidase-tqjs be used throughout the draft labels and labeling.

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/s/

CARLOS M MENA-GRILLASCA
06/28/2024 09:36:41 AM

CHI-MING TU
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PROPRIETARY NAME MEMORANDUM

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

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

Date of This Review:	February 6, 2024
Application Type and Number:	BLA 761347
Product Name, Dosage Form, and Strength:	Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs) Injection, 1,875 mg and 30,000 units/15 mL (125 mg and 2,000 units/mL)
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech Inc. (Genentech)
PNR ID #:	2023-1044725466
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Tecentriq Hybreza, which was found conditionally acceptable under BLA 761347 on February 13, 2023.[a] Subsequently, on August 31, 2023, Genentech withdrew BLA 761347. Thus, with the BLA resubmission, Genentech submitted the proposed proprietary name, Tecentriq Hybreza, under BLA 761347 for re-review on November 15, 2023.[b] We note that all product characteristics remain the same.

2 DISCUSSION

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tecentriq Hybreza would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Tecentriq Hybreza. The Division of Oncology 2 (DO2) concurred with the findings of OPDP's assessment for Tecentriq Hybreza.

2.2 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, Tecentriq Hybreza, 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 January 30, 2024 search of USAN stems did not find any USAN stems in the proposed proprietary name, Tecentriq Hybreza.

2.2.1 COMMUNICATION OF DMEPA'S DETERMINATION

On February 6, 2024, DMEPA 2 communicated our determination to the Division of Oncology 2 (DO2).

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, Tecentriq Hybreza, is conditionally acceptable.

If you have any questions or need clarifications, please contact CAPT Latonia Ford, OSE project manager, at 4901.

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[a] Stewart, J. Proprietary Name Review for Tecentriq Hybreza (BLA 761347). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 FEB 13. PNR ID No. 2023-1044724846.

[b] Request for Proprietary Name Review. San Francisco (CA): Genentech Inc.; 2023 NOV 15. Available from: \\CDSESUB1\EVSPROD\bla761347\0030\m1\us\proprietary-name.pdf

3.1 COMMENTS TO GENENTECH INC.

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

If any of the proposed product characteristics as stated in your submission, received on November 15, 2023 are altered prior to approval of the marketing application, the name proprietary must be resubmitted for review.

4 REFERENCE

1. United States Adopted Names (USAN) Stems

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

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/s/

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SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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Date of This Review:	6/16/2023
Responsible OND Division:	Division of Oncology 2 (DO2)
Application Type and Number:	BLA 761347
Product Name and Strength:	Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs) injection 1,875 mg and 30,000 units per 15 mL (125 mg and 2,000 units per mL)
Product Type:	Multiple Ingredient Product
Applicant/Sponsor Name:	Genentech, Inc. (Genentech)
Nexus NPNS ID #:	2022-155
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD

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 761347.

1.1 Regulatory History

Genentech requested that the Agency designate a four-letter suffix for inclusion in the proper name.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

atezolizumab and hyaluronidase-tqjs

FDA generated a four-letter suffix, -tqjs. This suffix was evaluated using the principles described in the applicable guidance[a].

We determined that the FDA-generated suffix -tqjs, 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.

We acknowledge that the proposed product is composed of two active ingredients, 'atezolizumab' and ' hyaluronidase' . Since the product contains two active ingredients, the core name for this product is the core names of the two components, atezolizumab and hyaluronidase. We considered the placement of the suffix within the nonproprietary name (i.e., after the atezolizumab component of the core name vs. after the hyaluronidase component of the core name). We are concerned that placement of the suffix after the atezolizumab component could result in misinterpretation of the nonproprietary name. Since

[a] Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

atezolizumab and hyaluronidase are available as individual components, the nonproprietary name, atezolizumab-xxxx and hyaluronidase, could be misinterpreted as an order for the individual components versus the proposed fixed-combination product, which may lead to confusion and medication error. Thus, in this case, we determined that the suffix should be attached at the end of the core name of the product (atezolizumab and hyaluronidase) with a hyphen, consistent with recommendations provided in the applicable guidance[a]. This placement would also ensure visibility of the suffix within the nonproprietary name. Thus, we determined atezolizumab and hyaluronidase-tqjs will be the proper name designated in the license.

3 COMMUNICATION OF DMEPA 2 ANALYSIS

These findings were shared with OPDP. On June 15, 2023, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Oncology 2 (DO2) on June 16, 2023.

4 CONCLUSION

We find the suffix -tqjs acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to atezolizumab and hyaluronidase-tqjs. DMEPA 2 will communicate our findings to the Applicant via letter.

4.1 Recommendation for Genentech, Inc.

We find the nonproprietary name, atezolizumab and hyaluronidase-tqjs, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, atezolizumab and hyaluronidase-tqjs 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/

CARLOS M MENA-GRILLASCA
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PROPRIETARY NAME REVIEW

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

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

Date of This Review:	February 13, 2023
Application Type and Number:	BLA 761347 and IND 140100
Product Name and Strength:	Tecentriq Hybreza (atezolizumab and hyaluronidase-xxxx)[a] Injection, 1,875 mg and 30,000 units/15 mL (125 mg and 2,000 units/mL)
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech Inc. (Genentech)
PNR ID #:	2022-1044724846 (BLA 761347) 2022-1044724657 (IND 140100)
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD, BCCCP
DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, BCPS

[a] The proposed nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as "atezolizumab and hyaluronidase-xxxx" throughout this review in place of the nonproprietary name for this product.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tecentriq Hybreza, 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. Genentech submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

1.1 REGULATORY HISTORY

Tecentriq (atezolizumab) injection was initially approved on May 18, 2016 (BLA 761034) and on October 18, 2016 (BLA 761041) for intravenous administration in single-use vials. The Applicant now proposes a new multi-ingredient formulation of atezolizumab and hyaluronidase for subcutaneous injection. The hyaluronidase is a recombinant human hyaluronidase PH20 (rHuPH20).

Thus, Genentech submitted the name, Tecentriq Hybreza, for review under IND 140100 on June 30, 2022 and under BLA 761347 on November 15, 2022.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 15, 2022.

- Intended Pronunciation: te-SEN-trik hye-BREEZE-uh
- Active Ingredient: atezolizumab and hyaluronidase-xxxx
- Indication of Use:
  (b) (4)
  - Adjuvant Non-small cell lung cancer (aNSCLC)
  - Metastatic Non-small cell lung cancer (mNSCLC)
  - Extensive-stage small-cell lung cancer (ES-SCLC)
  - Hepatocellular carcinoma (HCC)
  - Melanoma
- Route of Administration: Subcutaneous
- Dosage Form: Injection
- Strength: 1,875 mg and 30,000 units/15 mL (125 mg and 2,000 units/mL)
- Dose and Frequency: The recommended dosage is 1,875 mg/30,000 units administered subcutaneously in the thigh over approximately (b) (4) minutes every 3 weeks.
- How Supplied: Each carton contains 1 single-dose vial.
- Storage: Refrigerated at 2° to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tecentriq Hybreza would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Tecentriq Hybreza. The Division of Oncology 2 (DO2) did not comment on the findings of OPDP's assessment for Tecentriq Hybreza.

2.2 SAFETY ASSESSMENT

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

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

Genentech indicated in their submission that the proposed proprietary name, Tecentriq Hybreza, is comprised of the root name, Tecentriq, which is an FDA approved name; and the modifier, 'Hybreza', which has been added to indicate the addition of hyaluronidase. The use of the rootname "Tecentriq" and modifier "Hybreza" is evaluated in Section 2.2.5.

2.2.3 Comments from Other Review Disciplines at Initial Review

The Division of Oncology 2 (DO2) did not forward any comments or concerns relating to Tecentriq Hybreza at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety practitioners participated in DMEPA's prescription studies for Tecentriq Hybreza. Two participants from the written portion of the study omitted the modifier and responded with "Tecentriq", which is a currently marketed product. We further evaluate the use of a modifier, and modifier omission and oversight in section 2.2.5 below.

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

[b] USAN stem search conducted on January 23, 2023.

2.2.5 Safety assessment of the root name and modifier

The proposed proprietary name is comprised of two words: the root name "Tecentriq" and the modifier "Hybreza". The single-ingredient atezolizumab product, Tecentriq, is available for intravenous administration in strengths of 840 mg/14 mL and 1,200 mg/20 mL. Genentech has developed a multi-ingredient formulation of atezolizumab and hyaluronidase for subcutaneous injection in the thigh and proposes to use the modifier "Hybreza" to indicate the addition of hyaluronidase. Our assessment finds the use of the modifier also differentiates this subcutaneous formulation from the currently marketed intravenous formulation of Tecentriq. Differences between the proposed subcutaneous formulation and the currently marketed intravenous formulation are listed in Table 1 below.

Table 1. Product Characteristics of Tecentriq and Tecentriq Hybreza

	Tecentriq[c]	**Tecentriq Hybreza (proposed)**
Active Ingredient	atezolizumab	atezolizumab and hyaluronidase-xxx
Indication	For the treatment patients with: Non-Small Cell Lung Cancer (NSCLC) Small Cell Lung Cancer (SCLC) Hepatocellular Carcinoma (HCC) Melanoma Alveolar Soft Part Sarcoma (ASPS)	For the treatment patients with: Non-Small Cell Lung Cancer (NSCLC) Small Cell Lung Cancer (SCLC) Hepatocellular Carcinoma (HCC) Melanoma Alveolar Soft Part Sarcoma (ASPS) (b) (4)
Route of Administration	Intravenous infusion	Subcutaneous injection (thigh only)
Strength	• 840 mg/14 mL (60 mg/mL) • 1,200 mg/20 mL (60 mg/mL)	1,875 mg and 30,000 units/15 mL (125 mg and 2,000 units/mL)

[c] Tecentriq. DailyMed. National Library of Medicine; January 2023. Available from https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=6fa682c9-a312-4932-9831-f286908660ee&type=pdf

Dose and Frequency	Adult NSCLC, SCLC, ASPS: • 840 every 2 weeks or • 1200 every 3 weeks or • 1680 every 4 weeks Pediatric ASPS: 15 mg/kg (up to a maximum 1,200 mg) every 3 weeks	The recommended dosage is 1,875 mg/30,000 units (1,875 mg atezolizumab and 30,000 units hyaluronidase) administered subcutaneously in the thigh over approximately (b) (4) minutes every 3 weeks.
Dosage Form	Injection	Injection
How Supplied	Single-dose vials: • 840 mg/14 mL (60 mg/mL) • 1,200 mg/20 mL (60 mg/mL)	1,875 mg and 30,000 units/15 mL (125 mg and 2,000 units/mL) in a single-dose vial
Storage:	Refrigerated at 2° to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.	Refrigerated at 2° to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

Given the Genentech's proposal to use Tecentriq as the root name with the addition of a modifier, we considered the following (addressed respectively below): (1) evaluation of the use of the same root name, (2) whether use of a modifier is sufficient to adequately distinguish the products, and (3) evaluation of the proposed modifier "Hybreza".

1. **Evaluation of the use of the same root name**

   Tecentriq has been marketed as the proprietary name for atezolizumab for injection since 2016. The proposed multi-ingredient product contains both atezolizumab and hyaluronidase. Because the proposed product shares the active ingredient atezolizumab and indications (NSCLC, SCLC, HCC, ASPS), the use of the same root name Tecentriq appears appropriate.

   Additionally, our routine postmarketing surveillance has not identified any signals attributed to name confusion involving Tecentriq. Thus, we do not object to the use of the root name, Tecentriq, for this product.

2. **Whether use of a modifier is sufficient to adequately distinguish the products**

   According to Genentech, the hyaluronidase acts as a permeation enhancer which allows subcutaneous administration of high drug volumes.[d] Therefore, if the intravenous formulation was inadvertently administered subcutaneously, there is the potential for injection site reactions and hypersensitivity reactions. Further, the volume of the intravenous formulation needed to achieve a dose equivalent to the subcutaneous dose

[d] Genentech, Inc. 2.4 Nonclinical Overview (rHuPH20). South San Francisco (CA): Genentech, Inc. 2022 NOV15. Available at \\CDSESUB1\EVSPROD\bla761347\0001\m1\us\proprietary-name.pdf.

would be more than twice that of the intended subcutaneous dose. Also, atezolizumab would be very slowly absorbed, which may lead to the potential for underdose as the peak concentration would not be achieved. On the other hand, if the subcutaneous formulation was inadvertently administered intravenously, it may lead to the potential for overdose.

Genentech proposes to differentiate the products by using a modifier in the proprietary name nomenclature. We considered the risk of name confusion if the modifier is dropped. We note that omission and oversight of modifiers is cited in literature as a common cause of medication error.[e] Although modifiers may be omitted, they can assist in differentiating products and may help to prevent potential selection errors when used. Postmarket experience shows that the introduction of product line extensions may result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. In this specific case, product characteristics like the dose, strength, and route of administration are different between Tecentriq and the proposed Tecentriq Hybreza (See Table 1 above). Additionally, injectable oncology drug products administered by healthcare professionals typically undergo independent double checks by two pharmacists in the usual clinical setting so the likelihood of both pharmacists overlooking the difference in dose, strength, and route is minimized.

An alternative to using a modifier to distinguish this product from the currently marketed products is to use a different root name. However, marketing the new product under a unique proprietary name also carries a risk of medication errors, such as therapeutic duplication and overdoses. Thus, we agree that a modifier may assist in differentiating between the intravenous and subcutaneous formulations.

3. Evaluation of the proposed modifier "Hybreza"

Genentech indicated that the modifier "Hybreza" is intended to indicate the addition of hyaluronidase. We find that the modifier "Hybreza" is novel and has no well understood standard meaning in drug nomenclature. It is reasonable to expect that, like any novel modifier, awareness among healthcare practitioners will increase with market uptake of the product. Additionally, we determined that the modifier does not contain any components such as USAN stem, route of administration, or dosage form that is misleading or can contribute to medication error. Thus, it appears to provide adequate differentiation between the currently marketed Tecentriq (single-ingredient product, fixed and weight-based dosing, and intravenous administration) and the proposed drug product (multiple-ingredient product, fixed dosing, and subcutaneous administration). Thus, we do not object to the modifier "Hybreza".

2.2.6 Communication of DMEPA's Determination

On February 13, 2023, DMEPA 2 communicated our determination to the Division of Oncology 2 (DO2).

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

3 CONCLUSION

The proposed proprietary name, Tecentriq Hybreza, is conditionally acceptable.

If you have any questions or need clarifications, please contact Latonia Ford, OSE project manager, at 301-796-4901.

3.1 COMMENTS TO GENENTECH INC.

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

If any of the proposed product characteristics as stated in your submission, received on November 15, 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. [f]

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

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

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

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

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

- Low similarity: combined match percentage score ≤54%.

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[g]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Tecentriq Hybreza Study (Conducted on December 29, 2022)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order: Tecentriq Hybreza 1875mg and 30,000units/15ml SQ over 7 minutes every 3 weeks	Tecentriq Hybreza Bring to clinic. Dispense 1
Outpatient Prescription: Patient _____ Date 12-29-22 Address _____ ℞ Tecentriq Hybreza Bring to clinic #1 MEDWATCH 1-800-FDA-1088 Refill(s):_____ Dr. OS DEA No._____ Address _____ Telephone _____	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Tecentriq Hybreza	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Tecentriq Hybreza

As of Date 1/23/2023

259 People Received Study

90 People Responded

Study Name: Tecentriq Hybreza

Total	22	25	19	24	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
TACENTRIC HYBREEZA	0	0	1	0	1
TACENTRIC HYBRIZA	0	0	1	0	1
TASCENTRIC HYBREZA	0	0	1	0	1
TECENTINQ HYBREZA	1	0	0	0	1
TECENTREQ HYBRIZA	0	0	1	0	1
TECENTRI HYBREEZA	0	0	1	0	1
TECENTRIC HYBREEZA	0	0	1	0	1
TECENTRIC HYPREEZA	0	0	1	0	1
TECENTRIQ	1	0	0	1	2
TECENTRIQ HYBREEZA	0	0	3	0	3
TECENTRIQ HYBRERA	6	0	0	0	6
TECENTRIQ HYBREZA	13	25	0	21	59
TECENTRIQ HYBRISA	0	0	1	0	1
TECENTRIQ HYDREZA	0	0	0	1	1
TECENTRIQ HYLEREZA	0	0	0	1	1
TECENTRIQ HYLOREA	1	0	0	0	1
TESENTRIC HYBREEZA	0	0	1	0	1
TESENTRIC HYBREZA	0	0	1	0	1
TESENTRIC HYBRIZA	0	0	1	0	1
TESENTRIC HYPRISA	0	0	1	0	1
TESENTRIK HYBREEZA	0	0	2	0	2
TESENTRIQU IBREEZA	0	0	1	0	1
TISCENTRICHIBRIZA	0	0	1	0	1

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/s/

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