CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761420Orig1s000

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)

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

Date of This Review:	9/5/2024
Responsible OND Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	BLA 761420
Product Name and Strength:	Avtozma (tocilizumab-anoh) injection Vial: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL) Prefilled syringe and Autoinjector: 162 mg/0.9 mL
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Celltrion, Inc. (Celltrion)
FDA Received Date:	January 26, 2024
Nexus NPNS ID #:	2024-229
DMEPA 2 Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

1 PURPOSE OF REVIEW

This review summarizes our evaluation of the four-letter suffixes proposed by Celltrion for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761420.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On January 26, 2024, Celltrion submitted a list of six suffixes, in their order of preference, to be used in the nonproprietary name of their product[a]. Celltrion also provided their evaluation of the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Celltrion:

Table 1. Suffixes submitted by Celltrion***

1.	anoh
2.	(b) (4)
3.	
4.	
5.	
6.	

We reviewed Celltrion's proposed suffixes in the order of preference listed by Celltrion, along with the supporting data they submitted, using the principles described in the applicable guidance.[b]

[a] Nonproprietary Name Review Request and Supporting Analysis BLA 761420. Incheon (Republic of Korea): Celltrion Inc.; 2024 Jan 26. Available from: \\CDSESUB1\EVSPROD\bla761420\0001\m1\us\nonproprietary-name.pdf

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

2.1 tocilizumab-anoh

Celltrion's first proposed suffix, -anoh, is comprised of four distinct letters.

We determined that the proposed suffix -anoh, 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 September 5, 2024, OPDP did not identify any concerns that would render this proposed suffix unacceptable. DMEPA 1 also communicated our findings to the Division of Rheumatology and Transplant Medicine (DRTM) on September 5, 2024.

4 CONCLUSION

We find Celltrion's proposed suffix -anoh acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to tocilizumab-anoh. DMEPA 1 will communicate our findings to the Applicant via letter.

4.1 Recommendations for Celltrion, Inc.

We find the nonproprietary name, tocilizumab-anoh, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, tocilizumab-anoh 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 your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your 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
09/05/2024 02:40:00 PM

MISHALE P MISTRY
09/30/2024 11:28:50 AM

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 public***

Date of This Review:	April 24, 2024
Application Type and Number:	BLA 761420
Product Name, Dosage Form, and Strength:	Avtozma (tocilizumab-xxxx)[a] injection, Single-dose vial: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL); Prefilled syringe and prefilled pen: 162 mg/0.9 mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Celltrion (Celltrion)
PNR ID #:	2024-1044725610
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader (Acting):	Damon Birkemeier, PharmD, FISMP, NREMT
DMEPA 1 Associate Director for Nomenclature & Labeling:	Idalia E. Rychlik, PharmD

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder tocilizumab-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

Table of Contents

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Celltrion previously submitted the proposed proprietary name, Avtozma, under IND 153821 on April 10, 2023, and we found the name conditionally acceptable on October 5, 2023.[b]

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 5, 2024.[c]

Table 1. Relevant Product Information for Avtozma	
Intended pronunciation:	av toze' mah
Nonproprietary name:	tocilizumab-xxxx
Indication:	**Rheumatoid Arthritis (RA)** • Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs). **Giant Cell Arteritis (GCA)** • Adult patients with giant cell arteritis. **Polyarticular Juvenile Idiopathic Arthritis (PJIA)** • Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis. **Systemic Juvenile Idiopathic Arthritis (SJIA)** • Patients 2 years of age and older with active systemic juvenile idiopathic arthritis. **Coronavirus Disease 2019 (COVID-19)** • Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

[b] McMillan, T. Proprietary Name Review for Avtozma (IND 153821). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 OCT 05. PNR ID No. 2023-1044725088.

[c] Prescribing Information for Avtozma (tocilizumab-xxxx) BLA 761420. Durham (NC): Celltrion; 2024 JAN 26. Available from: \\Cdsesub1\evsprod\BLA761420\0001\m1\us\draft-labeling-text-avtozma.docx.

<table>
<tr><th colspan="2">Table 1. Relevant Product Information for Avtozma</th></tr>
<tr><td>Dosage Form:</td><td>injection</td></tr>
<tr><td>Strength:</td><td>Single-dose vial: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL); Prefilled syringe and prefilled pen: 162 mg/0.9 mL</td></tr>
<tr><td>Route of administration:</td><td>Intravenous infusion and subcutaneous injection</td></tr>
<tr><td>Dose and frequency:</td><td>
<u>Rheumatoid Arthritis</u>
Recommended Adult Intravenous Dosage:
When used in combination with DMARDs or as monotherapy the recommended starting dose is 4 mg per kg every 4 weeks followed by an increase to 8 mg per kg every 4 weeks based on clinical response.
Recommended Adult Subcutaneous Dosage:
<table>
<tr><td>Patients less than 100 kg weight</td><td>162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response</td></tr>
<tr><td>Patients at or above 100 kg weight</td><td>162 mg administered subcutaneously every week</td></tr>
</table>
<u>Giant Cell Arteritis</u>
Recommended Adult Intravenous Dosage:
The recommended dose is 6 mg per kg every 4 weeks in combination with a tapering course of glucocorticoids. AVTOZMA can be used alone following discontinuation of glucocorticoids.
Recommended Adult Subcutaneous Dosage:
The recommended dose is 162 mg given once every week as a subcutaneous injection, in combination with a tapering course of glucocorticoids.
A dose of 162 mg given once every other week as a subcutaneous injection, in combination with a tapering course of glucocorticoids, may be prescribed based on clinical considerations.
AVTOZMA can be used alone following discontinuation of glucocorticoids.
<u>Polyarticular Juvenile Idiopathic Arthritis</u>
<table>
<tr><th colspan="2">Recommended Intravenous PJIA Dosage Every 4 Weeks</th></tr>
<tr><td>Patients less than 30 kg weight</td><td>10 mg per kg</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>8 mg per kg</td></tr>
</table>
<table>
<tr><th colspan="2">Recommended Subcutaneous PJIA Dosage</th></tr>
<tr><td>Patients less than 30 kg weight</td><td>162 mg once every three weeks</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>162 mg once every two weeks</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th colspan="2">Table 1. Relevant Product Information for Avtozma</th></tr>
<tr><td></td><td>
<u>Systemic Juvenile Idiopathic Arthritis</u>
<table>
<tr><th colspan="2">Recommended Intravenous SJIA Dosage Every 2 Weeks</th></tr>
<tr><td>Patients less than 30 kg weight</td><td>12 mg per kg</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>8 mg per kg</td></tr>
</table>
<table>
<tr><th colspan="2">Recommended Subcutaneous SJIA Dosage</th></tr>
<tr><td>Patients less than 30 kg weight</td><td>162 mg every two weeks</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>162 mg every week</td></tr>
</table>
<u>Coronavirus Disease 2019</u>
The recommended dosage of AVTOZMA for adult patients with COVID-19 is 8 mg per kg administered by a 60-minute intravenous infusion.
</td></tr>
<tr><td>How Supplied:</td><td>
<u>For Intravenous Infusion</u>
AVTOZMA (tocilizumab-xxxx) injection is a preservative-free, sterile clear to slightly opalescent, colorless to pale yellow solution for intravenous infusion supplied in a single-dose vial packaged within cartons in the following strengths and packaging configurations:

80 mg/ 4 mL (20 mg/mL): carton of one vial and carton of 4 vials.
200 mg/ 10 mL (20 mg/mL): carton of one vial and carton of 4 vials.
400 mg/ 20 mL (20 mg/mL): carton of one vial and carton of 4 vials.

<u>For Subcutaneous Injection</u>
AVTOZMA (tocilizumab-xxxx) injection is supplied as a preservative-free, sterile, clear to slightly opalescent, colorless to yellow solution for subcutaneous administration. The following packaging configurations are available:

Each single-dose prefilled syringe delivers 162 mg/0.9 mL: carton of one syringe; carton of 4 syringes; carton of 3 packs of 4 syringes.
Each single-dose prefilled pen (autoinjector, AI) 162 mg/0.9 mL: carton of one syringe; carton of 4 syringes; carton of 3 packs of 4 syringes.

</td></tr>
</table>

Table 1. Relevant Product Information for Avtozma	
Storage:	Do not use beyond expiration date on the container, package, prefilled syringe, or autoinjector. AVTOZMA must be refrigerated at 36°F to 46°F (2°C to 8°C). Do not freeze. Protect the vials, syringes, and autoinjectors from light by storage in the original package until time of use, and keep syringes and autoinjectors dry. Once removed from the refrigerator, the prefilled syringe and autoinjector can be stored up to 3 weeks at or below 77°F (25°C). The prefilled syringe and autoinjector must always be kept in the carton.
Reference Product:	Avtozma (tocilizumab-xxxx) is a proposed interchangeable to US-licensed Reference Product, Actemra (tocilizumab) BLA 125276 and BLA 125472

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Avtozma 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 Avtozma. The Division of Rheumatology and Transplant Medicine (DRTM) noted that *"the proposed name looks and sounds very similar to Actemra and could easily be confused for the reference product when called into a pharmacy or if written on a prescription pad. We would ask OPDP to consider this."*

On April 11, 2024, OPDP stated they maintain a non-objection to the proposed proprietary name, Avtozma. OPDP deferred the safety evaluation to DMEPA 1.

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Celltrion did not provide a derivation or intended meaning for the proposed proprietary name, Avtozma, in their submission. This proprietary name is comprised of a single word that does not

[d] USAN stem search conducted on February 26, 2024.

contain any components (i.e., a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

On February 29, 2024, the Division of Rheumatology and Transplant Medicine (DRTM) noted that *"the proposed name looks and sounds very similar to Actemra and could easily be confused for the reference product when called into a pharmacy or if written on a prescription pad."* This name pair has sufficient phonetic and orthographic differences, as supported by a combined Phonetic and Orthographic Computer Analysis (POCA) score of 52%, suggesting low similarity between the names Avtozma and Actemra. Based on these factors, we determined the risk for a medication error between this name pair is adequately minimized. We evaluate the name Actemra in Appendix F.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Seventy-eight (n=78) practitioners participated in DMEPA's prescription simulation studies for Avtozma. 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[e] identified twenty-six (n=26) names with a combined score of ≥55% or an individual orthographic or phonetic score of ≥70%. We had identified and evaluated all 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 did not identify any names not previously analyzed.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from DRTM. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

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

[e] POCA search conducted on February 26, 2024 in version 5.5.

2.2.7 SAFETY ANALYSIS OF NAMES WITH POTENTIAL ORTHOGRAPHIC, SPELLING, AND PHONETIC SIMILARITIES

Our analysis of the one name contained in Table 2 determined that the name will not pose a risk for confusion with Avtozma as described in Appendices C through H.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On April 9, 2024, DMEPA 1 communicated our determination to the Division of Rheumatology and Transplant Medicine (DRTM).

3 CONCLUSION

The proposed proprietary name, Avtozma, is conditionally acceptable.

If you have any questions or need clarifications, please contact Davis Mathew, OSE project manager, at 240-402-4559.

3.1 COMMENTS TO CELLTRION

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

If any of the proposed product characteristics as stated in your submission, received on February 5, 2024 are altered prior to approval of the marketing application, the proprietary name must be resubmitted for review.

4 REFERENCES

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.

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 https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms).

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).

Purple Book

The Purple Book is an online database that contains information about biological products, including biosimilar and interchangeable biological products, licensed (approved) by the FDA under the Public Health Service (PHS) Act. See Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, available at https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or.

Division of Medication Errors Prevention and Analysis pending proprietary name requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis.

5 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, the Office of Prescription Drug Promotion (OPDP) assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by the Office of Non-Prescription Drugs (ONPD). OPDP or ONPD 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 ONPD 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 3*. 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]

*Table 3. 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.

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

*Table 3. 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 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, Purple Book, 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 4-6) 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 4).
- 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[9]. 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 5).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA also conducts 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), Office of Generic Drugs (OGD), and/or Office of Pharmaceutical Quality (OPQ) 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-

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

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 OPQ 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 Safety Evaluator 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 4. 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>
<tr><th colspan="3">Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).</th></tr>
<tr><td>Step 1</td><td colspan="2">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</td></tr>
<tr><td>Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.</td></tr>
<tr><td></td><td>Orthographic Checklist (Y/N to each question)
• Do the names begin with different first letters?
• Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.
• Are the lengths of the names dissimilar* when scripted?
• *FDA considers the length of names different if the names differ by two or more letters.
• Considering variations in scripting of some letters (such as z and f), is there a different number or</td><td>Phonetic Checklist (Y/N to each question)
• Do the names have different number of syllables?
• Do the names have different syllabic stresses?
• Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
• Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤69%).**		
	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?	

Table 6. 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. Avtozma Study (Conducted on 2/16/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order: Avtozma 4mg/kg intravenous infusion today	Avtozma Inject 162 mg subQ once a week Dispense #4
Outpatient Prescription: Avtozma Inject 162mg Sub-Q once a week #4	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Avtozma	

Study Name: Avtozma - 2024-02-16 People Received Study: 164 People Responded: 78					
Total	20	20	20	18	78
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
ABTOSEMA	0	0	1	0	1
AFTOZA	0	0	1	0	1
AFTOZMA	0	0	5	0	5
AQNEURSA	0	0	1	0	1
AUTOZMA	8	0	0	0	8
AVITOSMA	0	0	1	0	1
AVTOSMA	0	0	1	0	1
AVTOZIMA	0	1	0	0	1
AVTOZMA	12	19	10	18	59

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is **≥70%)** – N/A

APPENDIX D. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with no overlap or numerical similarity in Strength and/or Dose – N/A

APPENDIX E. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with overlap or numerical similarity in Strength and/or Dose – N/A

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is **≤54%)**

No.	Name	POCA Score (%)
1.	Actemra	52

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[h]. – N/A

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

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/

SARAH K VEE
04/24/2024 08:48:22 AM

DAMON A BIRKEMEIER
04/24/2024 09:00:13 AM

IDALIA E RYCHLIK
04/24/2024 11:34:53 AM