CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761275Orig1s000

PROPRIETARY NAME REVIEW(S)

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:	December 20, 2023
Application Type and Number:	BLA 761275
Product Name and Strength:	Tyenne (tocilizumab-aazg) injection 162 mg/0.9 mL (prefilled syringe and autoinjector presentations); 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) (vial presentations)
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Fresenius Kabi (Fresenius Kabi)
PNR ID #:	2023-1044725366
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tyenne, 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. Fresenius Kabi did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Fresenius Kabi previously submitted the proposed proprietary name, Tyenne*** under BLA 761275 on September 12, 2022. We found the name, Tyenne *** conditionally acceptable.[a] However, on May 31, 2023, BLA 761275 received a complete response.

Thus, Fresenius Kabi submitted the name, Tyenne, for review on September 28, 2023 under BLA 761275.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on September 28, 2023.

- Intended Pronunciation: tye en'
- Nonproprietary Name: tocilizumab-aazg
- Indication of Use:
    - 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.
- Route of Administration: intravenous infusion and subcutaneous injection
- Dosage Form: injection
- Strength: 162 mg/0.9 mL (prefilled syringe and autoinjector presentations); 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) (vial presentations)
- Dose and Frequency:

  Rheumatoid Arthritis

[a]McMillan, T. Proprietary Name Review for Tyenne (BLA 761275). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 NOV 29. PNR ID No. 2022-1044724750.

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:

Patients less than 100 kg weight	162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response
Patients at or above 100 kg weight	162 mg administered subcutaneously every week

Giant Cell Arteritis

Recommended Adult Intravenous Dosage:

The recommended dose is 6 mg per kg every 4 weeks in combination with a tapering course of glucocorticoids. TYENNE 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.

TYENNE can be used alone following discontinuation of glucocorticoids.

Polyarticular Juvenile Idiopathic Arthritis

Recommended Intravenous PJIA Dosage Every 4 Weeks	
Patients less than 30 kg weight	10 mg per kg
Patients at or above 30 kg weight	8 mg per kg

Recommended Subcutaneous PJIA Dosage	
Patients less than 30 kg weight	162 mg once every three weeks
Patients at or above 30 kg weight	162 mg once every two weeks

Systemic Juvenile Idiopathic Arthritis

Recommended Intravenous SJIA Dosage Every 2 Weeks	
Patients less than 30 kg weight	12 mg per kg
Patients at or above 30 kg weight	8 mg per kg

Recommended Subcutaneous SJIA Dosage	
Patients less than 30 kg weight	162 mg every two weeks
Patients at or above 30 kg weight	162 mg every week

- How Supplied:
  - Carton containing one single-dose vial: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL)
  - Carton containing one prefilled syringe: 162 mg/0.9 mL.
  - Carton containing one autoinjector: 162 mg/0.9 mL.
- Storage: Do not use beyond expiration date on the container, package, prefilled syringe, or autoinjector. TYENNE must be refrigerated at 36°F to 46°F (2ºC to 8ºC). Do not freeze. A single prefilled syringe (or autoinjector) may be stored at (b) (4) (b) (4) 77°F (25°C) for a single period of up to 14 days. . Protect the vials, syringes, and autoinjectors from light by storage in the original package until time of use and keep syringes and autoinjectors dry.
- Tyenne (tocilizumab-aazg) is a proposed biosimilar to US-licensed Reference Product, Actemra (tocilizumab) BLA 125276 and BLA 125472.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The determined that Tyenne 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 Tyenne. The Division of Rheumatology and Transplant Medicine (DRTM) did not comment on the findings of OPDP's assessment for Tyenne.

2.2 SAFETY ASSESSMENT

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

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

Fresenius Kabi did not provide a derivation or intended meaning for the proposed proprietary name, Tyenne, in their submission. This proprietary name is comprised of a single word that does not 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 November 2, 2023, the Division of Rheumatology and Transplant Medicine (DRTM) did not forward any comments or concerns relating to Tyenne at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Sixty-five (n=65) practitioners participated in DMEPA's prescriptiotn studies for Tyenne. One inpatient participant responded "Tylenol". The participant stated that they would not confuse the name but wanted to note that the study name was similar to "Tylenol". We previously reviewed Tylenol (combined POCA score of 61%) and determined that the name pair has sufficient orthographic and phonetic differences.[c]

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

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified 52 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed, and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified one name not previously analyzed. These names are included in Table 1 below.

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[b] USAN stem search conducted on October 11, 2023.

[c] McMillan, T. Proprietary Name Review for Tyenne (BLA 761275). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 NOV 29. PNR ID No. 2022-1044724750.

[d] POCA search conducted on October 11, 2023 in version 5.2.

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 ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	1
Low similarity name pair: combined match percentage score ≤54%	0

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

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

2.2.8 Communication of DMEPA's Determination

On December 20, 2023, DMEPA 1 communicated our determination to the Division of Rheumatology and Transplant Medicine (DRTM).

3 CONCLUSION

The proposed proprietary name, Tyenne, 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 FRESENIUS KABI

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

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, 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[f]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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

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

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

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

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

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

   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.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
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 <u>with</u> overlapping or similar strengths or doses.

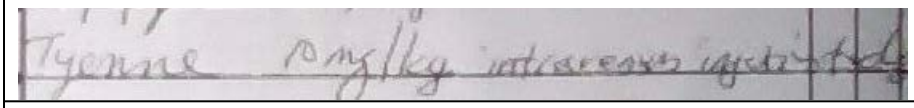
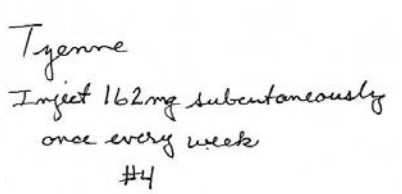
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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 **≤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. Tyenne Study (Conducted on October 10, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Tyenne	Tyenne Inject 162 mg subcutaneously once every week #4

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Tyenne

People Received Study: 229

People Responded: 65

Total	20	16	13	16	65
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
TAIEN	0	0	1	0	1
TAIYAN	0	0	1	0	1
TYAN	0	0	4	0	4
TYEN	0	0	3	0	3
TYEND	0	0	1	0	1
TYENNE	19	15	1	16	51
TYENVE	0	1	0	0	1
TYIN	0	0	2	0	2
TYLENOL	1	0	0	0	1

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%) – 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].

No.	Name	POCA Score (%)
1.	(b) (4) ***	56

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

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/s/

SARAH K VEE
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12/21/2023 09:16:09 AM
Signed on behalf of Idalia Rychlik

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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)

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

Date of This Review:	12/14/2023
Responsible OND Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	BLA 761275
Product Name and Strength:	Tyenne (tocilizumab-aazg) injection Vials: 80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL (20 mg/mL)
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Fresenius Kabi USA, LLC (Fresenius)
Nexus NPNS ID #:	2023-193
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 proposed suffix, -aazg, for BLA 761275, which was found conditionally acceptable on March 2, 2023[a], for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761275.

1.1 Regulatory History

The proposed four-letter suffix, -aazg, was found conditionally acceptable for BLA 761275 on March 2, 2023. However, BLA 761275 received a Complete Response (CR) letter on May 31, 2023[b]. Thus, Fresenius submitted a Class 2 Resubmission on September 5, 2023.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the proposed four-letter suffix, -aazg, using the principles described in the applicable guidance[c].

We note that the letters 'aa' in the suffix represent the medical abbreviations for 'affected area' and 'of each'. We considered whether the inclusion of the letters 'aa' within the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

We determined that the proposed suffix -aazg, 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 13, 2023, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 1 also communicated our findings to the Division of Rheumatology and Transplant Medicine (DRTM) on December 14, 2023.

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[a] Mena-Grillasca, C. Nonproprietary Name Suffix Review for tocilizumab-aazg (BLA 761275). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 Mar 02. Nexus NPNS ID No.: 2022-100.

[b] Glaser, R. Complete Response (BLA 761275). Silver Spring (MD): FDA, CDER, OND, DRTM (US); 2023 May 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 -aazg acceptable and recommend the nonproprietary name tocilizumab-aazg be used throughout the draft labels and labeling.

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
12/14/2023 10:46:28 AM

MISHALE P MISTRY
12/14/2023 11:07:55 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:	3/2/2023
Responsible OND Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	BLA 761275
Product Name and Strength:	Tyenne (tocilizumab-aazg) injection Vials: 80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL (20 mg/mL) Prefilled Syringe: 162 mg/0.9 mL
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Fresenius Kabi USA, LLC (Fresenius)
FDA Received Date:	May 31, 2022
Nexus NPNS ID #:	2022-100
DMAMES 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 Fresenius for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761275.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On May 31, 2022, Fresenius submitted a list of 10 suffixes, in their order of preference, to be used in the nonproprietary name of their product[a]. Fresenius also provided findings from an external study conducted by (b) (4) [b], evaluating the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Fresenius:

Table 1. Suffixes submitted by Fresenius***	
1.	(b) (4)
2.	aazg
3.	(b) (4)
4.	
5.	
6.	
7.	
8.	
9.	
10.	

[a] Request for Nonproprietary Naming – Suffixes BLA 761275. Lake Zurich (IL): Fresenius Kabi USA, LLC; 2022 May 31. Available from: file://CDSESUB1/evsprod/bla761275/0001/m1/us/118-prop-names/request-for-nonproprietary-naming-suffixes.pdf

[b] Request for Nonproprietary Naming – Suffixes – Safety Report. (b) (4); 2022 May 31. Available from: file://CDSESUB1/evsprod/bla761275/0001/m1/us/118-prop-names/request-for-nonproprietary-naming-suffixes-safety-report.pdf

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

2.1 tocilizumab-(b) (4)

Fresenius's first proposed suffix, -(b) (4), but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

However, the proposed suffix -(b) (4). This similarity is supported by the FDA's Phonetic and Orthographic Computer Analysis (POCA) system, which calculates an orthographic POCA score of 75%, indicating that the suffixes are orthographically highly similar. Therefore, the proposed suffix -(b) (4) is too similar to an approved proper name suffix and is therefore inconsistent with the principle outlined in section VI of the guidance[a] that a suffix should not be too similar to any other FDA-designated suffix.

We note that our conclusion differs from that of (b) (4) assessment. However, they did not identify and evaluate the similarity between the proposed suffix -(b) (4) and the FDA-designated suffix -(b) (4).

2.2 tocilizumab-aazg

Fresenius's second proposed suffix, -aazg, is comprised of 3 distinct letters (a, z, g). We note that the letters 'aa' in the suffix represent the medical abbreviation for 'affected area' and 'of each'. We considered whether the inclusion of the letters 'aa' within the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

We determined that the proposed suffix -aazg, 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

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

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 March 1, 2023, 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 March 2, 2023.

4 CONCLUSION

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

4.1 Recommendations for Fresenius Kabi USA, LLC

We find the nonproprietary name, tocilizumab-aazg, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, tocilizumab-aazg 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.

We also note that your first proposed suffix is unacceptable for the following reasons:

1. -(b) (4)

   We find your first proposed suffix, -(b) (4), unacceptable. The proposed suffix, -(b) (4) . This similarity is supported by the FDA' s Phonetic and Orthographic Computer Analysis (POCA) system, which calculates an orthographic POCA score of 75%, indicating that the suffixes are orthographically highly similar. Therefore, the proposed suffix -(b) (4) is too similar to an approved proper name suffix and is therefore inconsistent with the principles outlined in section VI of the guidance[a].

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

We note that our conclusion differs from that of the external study you submitted from [redacted]. However, [redacted] did not identify and evaluate the similarity between the proposed suffix -[redacted] and the FDA-designated suffix -[redacted].

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
03/02/2023 04:56:25 PM

MISHALE P MISTRY
03/03/2023 09:31:47 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:	November 29, 2022
Application Type and Number:	BLA 761275
Product Name and Strength:	Tyenne (tocilizumab-xxxx) [a] Injection 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Fresenius Kabi SwissBioSim GmbH (Fresenius Kabi)
PNR ID #:	2022-1044724750
DMEPA 1 Safety Evaluator:	Teresa McMillan, PharmD
DMEPA 1 Team Leader:	Idalia Rychlik, PharmD
DMEPA 1 Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD

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

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tyenne, 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. Fresenius Kabi submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

1.1 REGULATORY HISTORY

Fresenius Kabi previously submitted the proposed proprietary name, (b) (4) *** on May 14, 2022, January 18, 2022, and on May 31, 2022. However, under IND 129965 and BLA 761275 on November 2, 2021 and on August 9, 2022, we found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with the marketed proprietary name, (b) (4) .[b]

Thus, Fresenius Kabi submitted the name, Tyenne, for review on September 12, 2022.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on September 12, 2022.

- Intended Pronunciation: tye en'
- Nonproprietary Name: tocilizumab-xxxx
- Indication of Use:

  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

  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.
- Route of Administration: Intravenous or Subcutaneous injection
- Dosage Form: Injection

[b] McMillan, T. Proprietary Name Review for Tyenne (IND 129965 and BLA 761275). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 AUG 19. PNR ID No. 2022-1044724398 and 2022-1044724610.

- Strength: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL
- Dose and Frequency:

Rheumatoid Arthritis 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:

Patients less than 100 kg weight	162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response
Patients at or above 100 kg weight	162 mg administered subcutaneously every week

Giant Cell Arteritis Recommended Adult Subcutaneous Dosage:

The recommended dose for adult patients with GCA 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.

Can be used alone following discontinuation of glucocorticoids.

Subcutaneous formulation is not intended for intravenous administration.

Polyarticular Juvenile Idiopathic Arthritis

Recommended Intravenous PJIA Dosage Every 4 Weeks	
Patients less than 30 kg weight	10 mg per kg
Patients at or above 30 kg weight	8 mg per kg

Recommended Subcutaneous PJIA Dosage	
Patients less than 30 kg weight	162 mg once every three weeks

Patients at or above 30 kg weight	162 mg once every two weeks

Systemic Juvenile Idiopathic Arthritis

Recommended Intravenous SJIA Dosage Every 2 Weeks	
Patients less than 30 kg weight	12 mg per kg
Patients at or above 30 kg weight	8 mg per kg

Recommended Subcutaneous SJIA Dosage	
Patients less than 30 kg weight	162 mg every two weeks
Patients at or above 30 kg weight	162 mg every week

- How Supplied:

  Injection is a preservative-free, sterile clear and colorless to pale yellow solution. The following packaging configurations are available:

  For Intravenous Infusion

  Single-Dose Vial

  Each carton contains one vial. Each vial is supplied as 80 mg/4 mL (NDC xxxxx-xxx-xx), 200 mg/10 mL (NDC xxxxx-xxx-xx), and 400 mg/20 mL (NDC xxxxx-xxx-xx) Solution for further dilution prior to intravenous infusion. The vial stopper is (b) (4).

  For Subcutaneous Injection

  Prefilled Syringe

  Each carton contains (b) (4) a single-dose prefilled syringe delivering 162 mg/0.9 mL. The syringe plunger stopper and needle cover are not made with natural rubber latex. The NDC number is xxxxx-xxx-xx.

  Autoinjector

  Each carton contains (b) (4) a single-dose autoinjector delivering 162 mg/0.9 mL. The syringe plunger stopper and needle cover are (b) (4). The NDC number is xxxxx-xxx-xx.

- Storage: Do not use beyond expiration date on the container, package, prefilled syringe, or autoinjector. Must be refrigerated at 36°F to 46°F (2°C to 8°C). Do not freeze. A single prefilled syringe (or autoinjector) may be stored at (b) (4) 77°F (25°C) for a single period of up to 14 days. (b) (4) Protect the vials, syringes, and autoinjectors from light by storage in the original package until time of use, and keep syringes and autoinjectors dry.
- Reference Listed Drug/Reference Product: Actemra (tocilizumab) BLA 125276

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tyenne 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 Tyenne. The Division of Rheumatology and Transplant Medicine (DRTM) concurred with the findings of OPDP's assessment for Tyenne.

2.2 SAFETY ASSESSMENT

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

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

Fresenius Kabi did not provide a derivation or intended meaning for the proposed proprietary name, Tyenne, in their submission. This proprietary name is comprised of a single word that does not 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 October 4, 2022, the Division of Rheumatology and Transplant Medicine (DRTM) did not forward any comments or concerns relating to Tyenne at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-seven practitioners participated in DMEPA's prescription studies for Tyenne. In the Computerized Physician Order Entry (CPOE) study, one participant's response overlapped with

[c] USAN stem search conducted on September 22, 2022.

the marketed product, Tyvaso. It appears the CPOE participant entered an incorrect sequence of letters, 'T-Y-V-A' when searching for the study name. As a result, the CPOE generated a pick list that did not contain Tyenne as a choice. After 28 seconds, the participant proceeded to incorrectly select the name Tyvaso as their response. Thus, in this case, it appears the participant attempted to select an answer that was closest to the response needed given the goal of the simulated study. We evaluated the name pair further and determined that this name pair is not likely to be confused.

This name pair has sufficient phonetic and orthographic differences, with a combined POCA score of 43%, suggesting low similarity between Tyenne and Tyvaso (see Appendix F). Specifically, the infixes/suffixes (enne vs. vaso) of the name pair provides sufficient orthographic differences. Phonetically, Tyvaso has an additional syllable and the second/third syllables sound different (en' vs. vā-sō). Additionally, we note the following differences in product characteristics that could help mitigate the possibility of error:

- Tyenne is an injection given subcutaneously and/or intravenously whereas Tyvaso is a solution for oral inhalation and Tyvaso DPI is an inhalation powder, both of which are administered via oral inhalation. Therefore, there is no overlap in dosage form or route of administration. Tyvaso is to be used with the Tyvaso Inhalation system and Tyvaso DPI cartridges are to be used with the Tyvaso DPI inhaler.
- Tyenne is available in multiple strengths (80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL). Tyvaso is available in a single strength (2.9 mL ampule containing 1.74 mg treprostinil (0.6 mg per mL)) and Tyvaso DPI is available in multiple strengths (16, 32, 48, or 64 mcg), none of which overlap with that of Tyenne.
- Tyvaso is administered as 3 inhalations (18 mcg) four times daily at one to two week intervals and may be increased to 9 to 12 breaths four times daily as a maintenance dose. Tyvaso DPI is administered as one 16 mcg cartridge per treatment session four times daily, increasing dosage by an additional 16 mcg per treatment session at approximately 1- to 2-week intervals to a target maintenance dosage of 48 mcg to 64 mcg per session. The doses of Tyvaso/Tyvaso DPI do not overlap with that of Tyenne (see Section 1.2 above).

Based on the aforementioned factors and differences in the product characteristics, we determined that the risk for a medication error between this name pair is adequately minimized.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified 52 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

[d] POCA search conducted on September 22, 2022 in version 4.5.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search, FDA Simulation Study, and (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	33
Low similarity name pair: combined match percentage score ≤54%	17

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

Our analysis of the 52 names contained in Table 1 determined none of the names will pose a risk for confusion with Tyenne as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On November 29, 2022, DMEPA 1 communicated our determination to the Division of Rheumatology and Transplant Medicine (DRTM).

3 CONCLUSION

The proposed proprietary name, Tyenne, 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 FRESENIUS KABI SWISSBIOSIM GMBH

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

If any of the proposed product characteristics as stated in your submission, received on September 12, 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 ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

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

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

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

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

[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 ≥ 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.

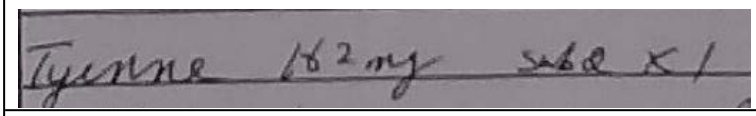
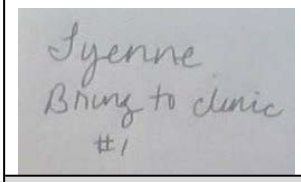
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Tyenne Study (Conducted on October 7, 2022)

Handwritten Medication Order/Prescription	**Verbal Prescription**
	Tyenne Bring to clinic #1
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Tyenne	

FDA Prescription Simulation Responses (Aggregate Report)

266 People Received Study
97 People Responded

Study Name: Tyenne

Total	**24**	**24**	**24**	**25**	
INTERPRETATION	**INPATIENT**	**CPOE**	**VOICE**	**OUTPATIENT**	**TOTAL**
FYENNE	0	0	0	1	1
HYEM	0	0	1	0	1
IYENNE	0	0	0	3	3
JYENNE	0	0	0	1	1
LYENNE	0	0	0	10	10
LYVENNE	0	0	0	1	1
S/J/TYENNE	0	0	0	1	1
TIAN	0	0	1	0	1
TIYEN	0	0	1	0	1
TYAM	0	0	1	0	1
TYAN	0	0	3	0	3

TYAYN	0	0	1	0	1
TYEM	0	0	7	0	7
TYEN	0	0	5	0	5
TYENNA	6	0	0	0	6
TYENNE	7	23	0	8	38
TYIEM	0	0	1	0	1
TYIN	0	0	2	0	2
TYINNE	9	0	0	0	9
TYRNNE	2	0	0	0	2
TYVASO	0	1	0	0	1
TYYEN	0	0	1	0	1

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

No.	**Proposed name:** Tyenne **Established name:** tocilizumab-xxxx **Dosage form:** Injection **Strength(s):** 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL **Usual Dose:** See Section 1.2	**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.	Tyenne	100	This name is the subject of this review.
2.	Tena	72 74-phonetic 70-ortho	Orthographically, the downstroke letter 'y' in the 2nd position of Tyenne, along with the difference in length of names (six letters vs. four letters) provide sufficient orthographic differences. Phonetically, the ending sounds of the 2nd syllables ('en' vs. 'na'), provide sufficient phonetic differences. The following product characteristics would help to mitigate the error: Tyenne is an injection given subcutaneously and/or intravenously once weekly or every two/four weeks vs. Tena is a brand of over the counter incontinence pads to be used as needed. When all of the aforementioned mitigations are considered in totality, we find the risk of confusion is adequately minimized in this case.

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

No.	**Proposed name:** Tyenne **Established name:** tocilizumab-xxxx **Dosage form:** Injection **Strength(s):** 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL **Usual Dose:** See Section 1.2	**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.	Twyneo	69 75-ortho	This name pair has sufficient orthographic and phonetic differences.
2.	Tenex	64 77-ortho	This name pair has sufficient orthographic and phonetic differences.
3.	Tencet	63 75-ortho	This name pair has sufficient orthographic and phonetic differences.
4.	Tydemy	62	This name pair has sufficient orthographic and phonetic differences.
5.	Tenake	61 71-ortho	This name pair has sufficient orthographic and phonetic differences.
6.	Tylenol	61	This name pair has sufficient orthographic and phonetic differences.
7.	Tyzine	59	Phonetically, the ending sounds of the 2nd syllables (‘en’ vs. ‘zeen’), provide some phonetic differences. The following product characteristics would help to mitigate the error: • Tyenne is an injection given subcutaneously and/or intravenously at doses of 4 mg, 8 mg, 10 mg, or 12 mg per kg every two/four weeks or 162 mg once weekly or every two/three/ (b) (4) weeks. • Tyzine is a nasal spray given intranasally at doses of 2 to 4 drops or 3 to 4 sprays instilled in each nostril as needed, never more often than every 3 hours. Less frequent administration is usually sufficient because relief is maintained for 4 hours

No.	**Proposed name:** Tyenne **Established name:** tocilizumab-xxxx **Dosage form:** Injection **Strength(s):** 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL (20 mg/mL), 162 mg/0.9 mL **Usual Dose:** See Section 1.2	**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**
			or longer in most cases, and often for as long as 8 hours.
8.	Ten-K	59 70-ortho	This name pair has sufficient orthographic and phonetic differences.
9.	Tremin	58	This name pair has sufficient orthographic and phonetic differences.
10.	Tretten	58	This name pair has sufficient orthographic and phonetic differences.
11.	Two-Dyne	58	This name pair has sufficient orthographic and phonetic differences.
12.	(b) (4)***	57	This name pair has sufficient orthographic and phonetic differences.
13.	Tin-Ben	56	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
1.	4-Cymene	54 71-ortho
2.	Cymene	54 71-ortho
3.	Ethylene	52 79-ortho
4.	Xylene	52 71-ortho
5.	Theanine	52 71-ortho
6.	Thypinone	50 70-ortho
7.	Trientine	50 70-ortho
8.	Tycolene	50 70-ortho
9.	Trevyent***	49 71-ortho

No.	Name	POCA Score (%)
10.	Entyce	50 71-ortho
11.	Hyteneze	48 71-ortho
12.	Rotenone	48 71-ortho
13.	Acetylene	46 73-ortho
14.	Atensine	46 73-ortho
15.	Ziana	46 Phono-70
16.	Tyvaso	43
17.	Ethylbenzene	43 72-ortho

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

No.	Name	POCA Score (%)	Failure preventions
1.	(b) (4) ***	63	(b) (4)
2.	Tylan	62	Veterinary product
3.	Trynate	59	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
4.	Tannate	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
5.	Rennet	58	Product is not a drug. It is an organic substance that contains the enzyme rennin.
6.	Tencon	57	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
7.	Tadenan	56	International product marketed in China.

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

No.	Name	POCA Score (%)
1.	Attane	60
2.	Kyleena	60
3.	Syeda	60
4.	Styrene	58
5.	Byetta	57
6.	1-Butene	56
7.	Beano	56
8.	C-Tanna 12	56
9.	Konyne 80	56
10.	Pheneen	56
11.	R-Tanna	56
12.	R-Tanna 12	56
13.	Senna S	56

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

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