CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216190Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	September 6, 2024
Application Type and Number:	NDA 216190
Product Name, Dosage Form, and Strength:	Ontralfy (tizanidine oral solution), 2 mg/5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Fidelity BioPharma Co. (Fidelity)
PNR ID #:	2024-1044725842
DMEPA 2 Safety Evaluator:	Rina Patel, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD
DMEPA 2 Associate Director for Nomenclature and Labeling:	Hina Mehta, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Ontralfy, 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. Fidelity referred to the previously submitted external name study, conducted by [redacted] (b) (4) for this proposed proprietary name. The submitted external name study was previously reviewed under NDA 216190 (see Section 1.1 below).

1.1 REGULATORY HISTORY

Fidelity previously submitted the proposed proprietary name, Ontralfy, under NDA 216190 on May 31, 2023, and we found the name conditionally acceptable on August 21, 2023.[b] However, NDA 216190 received a Complete Response (CR) on March 29, 2024. Thus, Fidelity resubmitted the name, Ontralfy, for review on June 12, 2024 as part of the response to the CR for NDA 216190. We note that all product characteristics remain the same.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission[c] received on May 31, 2023 (referred to in the June 12, 2024 Cover Letter[d]) and the prescribing information received on July 15, 2024[e].

Table 1. Relevant Product Information for Ontralfy	
Intended pronunciation:	on tral' fee
Active ingredient:	tizanidine
Indication:	[redacted] (b) (4) of spasticity
Dosage Form:	oral solution
Strength:	2 mg/5 mL
Route of administration:	oral

[a] Proprietary Name Safety Summary for ONTRALFY. [redacted] (b) (4) 2023 MAR 2023. Available from: \\CDSESUB1\EVSPROD\nda216190\0001\m1\us\118-proprietary-names\prop-name-safe-summary-ontralfy.pdf.

[b] Patel, R. Proprietary Name Review for Ontralfy (NDA 216190). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 AUG 21. PNR ID No. 2023-1044725163.

[c] Proprietary Name Review Request (NDA 216190 Ontralfy). New Haven (CT): Fidelity BioPharma Co.; 2023 MAY 31. Available from: \\CDSESUB1\EVSPROD\nda216190\0001\m1\us\118-proprietary-names\prop-name-review-req.pdf.

[d] Cover Letter – Resubmission and Request for Proprietary Name Review (NDA 216190 Ontralfy). New Haven (CT): Full Applicant/Sponsor name; 2024 JUN 12. Available from: \\CDSESUB1\EVSPROD\nda216190\0014\m1\us\12-cover-letters\cover-0014.pdf.

[e] Proposed prescribing information for Ontralfy. See link in Cover Letter – Labeling Resubmission. New Haven (CT): Fidelity BioPharma Co.; 2024 JUL 15. Available from: \\CDSESUB1\EVSPROD\nda216190\0015\m1\us\12-cover-letters\cover-0015.pdf.

Table 1. Relevant Product Information for Ontralfy	
Dose and frequency:	• Recommended starting dose: 2 mg (5 mL) every 6 to 8 hours as needed up to a maximum of 3 doses in 24 hours. • Dosage can be increased by 2 mg (5 mL) to 4 mg (10 mL) per dose, with 1 to 4 days between increases. • Total daily dose should not exceed 36 mg.
How Supplied:	473 mL filled into a 16 oz (b) (4) bottle with a child-resistant closure.
Storage:	Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]
Reference Listed Drug:	• Zanaflex (tizanidine hydrochloride) NDA 020397 • Zanaflex Capsules (tizanidine hydrochloride) NDA 021447

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Ontralfy would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Ontralfy. The Division of Neurology 1 (DN 1) did not comment on the findings of OPDP's assessment for Ontralfy.

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Fidelity did not provide a derivation or intended meaning for the proposed proprietary name, Ontralfy, in their submission. We note that the name contains the letter string 'tr' which is a medical abbreviation for the modifier 'time-release'. We previously assessed the use of 'tr', and we do not object to the inclusion of 'tr' within the proposed proprietary since our last review.[g]

[f] USAN stem search conducted on June 26, 2024.

[g] Patel, R. Proprietary Name Review for Ontralfy (NDA 216190). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 AUG 21. PNR ID No. 2023-1044725163.

Aside from 'tr', the proprietary name is comprised of a single word that does not contain any components (i.e., route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

The Division of Neurology 1 (DN 1) did not forward any comments or concerns relating to Ontralfy at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Ninety-five (95) practitioners participated in DMEPA's prescription studies for Ontralfy.

In the comments section of the Outpatient study, one respondent commented that the proprietary name is "very similar to [(b) (4)]***" which is a proposed proprietary name for another product also under review. Additionally, one respondent in the Computerized Prescription Order Entry (CPOE) study incorrectly selected the name Ontruzant. We further evaluated the name pairs Ontralfy vs. [(b) (4)] ** and Ontralfy vs. Ontruzant for risk of medication errors.

Ontralfy vs. [(b) (4)]***

Orthographically, [(b) (4)]*** contains the [(b) (4)] in the 2nd position, while Ontralfy contains the rounded letter 'n' in the same position. Additionally, Ontralfy contains the upstroke, cross-stroke letter 't' in the 3rd position while [(b) (4)] ** contains the [(b) (4)] in the same position. Further, [(b) (4)]*** contains only one [(b) (4)] [(b) (4)] in the suffix (6th position) while Ontralfy contains the upstroke letter 'l' in the 6th position immediately followed by another upstroke and optional downstroke/cross-stroke letter 'f' in the 7th position.

Phonetically, the names have a different number of syllables (3 vs. 4), and the ending of the first syllables (on vs. [(b) (4)]), the ending of the second syllables (tral' vs. [(b) (4)], and the entire third syllables (fee vs. [(b) (4)] sound different when spoken.

Although the strengths differ (2 mg/5 mL vs. [(b) (4)]), we acknowledge that both products are only available in a single strength; therefore, this information may not be included on a prescription. However, these products also differ in route of administration (oral vs. [(b) (4)]), dosage form (solution vs. [(b) (4)], dose in milligrams (2 mg up to 12 mg vs. [(b) (4)] mg), and frequency of administration (every 6 to 8 hours as needed vs. [(b) (4)] [(b) (4)] which provides additional differentiation if included on a prescription or order. Thus, in this specific case, the risk of name confusion between this name pair is minimized (see Appendix E).

Ontralfy vs. Ontruzant

We considered whether additional product characteristics would help differentiate the products during an electronic prescribing scenario. We note the dosage form (oral solution vs. for injection), route of administration (oral vs. intravenous infusion), strength (2 mg/5 mL vs. 150 mg and 420 mg), and frequency of administration (every 6 to 8 hours as needed vs. once

weekly or every 3 weeks) differ between the two products which are unlikely to be overlooked in an electronic prescribing scenario.

Additionally, Ontruzant is an injectable oncologic drug indicated for the treatment of HER2 - overexpressing breast cancer and the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma. Because injectable oncologic drugs administered by healthcare professionals typically undergo independent double checks by two pharmacists in the usual clinical setting, the likelihood of both pharmacists overlooking the differences in product characteristics is minimized.

Orthographically, the suffixes of the name pair (-alfy vs. -zant) differ. Specifically, Ontralfy contains the upstroke letter 'l' in the 6th position and the optional downstroke/cross-stroke letter 'f' in the 7th position, while Ontruzant contains the optional downstroke letter 'z' and rounded letter 'a' in the same positions. Additionally, Ontralfy contains the downstroke letter 'y' in the last position (8th position) while Ontruzant contains the upstroke, cross-stroke letter 't' in the last position. Phonetically, the ending of the second syllables (tral' vs. TROO) and the third syllables (fee vs. zahnt) sound different when spoken. When the above is considered in totality, we find the potential for name confusion with this name pair to be minimal (see Appendix E).

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

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search[h] identified 88 names with a combined score of ≥55% or an 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. This name is included in Table 2 below.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from our POCA search and the FDA Prescription Simulation Study. 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

[h] POCA search conducted on July 1, 2024 in version 5.9.

Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	2
Low similarity name pair: combined match percentage score ≤54%	1

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

Our analysis of the 3 names contained in Table 2 determined none of the names will pose a risk for confusion with Ontralfy as described in Appendices C through H.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On September 6, 2024, DMEPA 2 communicated our determination to the Division of Neurology 1 (DN 1).

3 CONCLUSION

The proposed proprietary name, Ontralfy, is conditionally acceptable.

3.1 COMMENTS TO FIDELITY BIOPHARMA CO.

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

If any of the proposed product characteristics as stated in your submission, received on May 31, 2023, and resubmission received on June 12, 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.[i]

*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.

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

- Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 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-

[j] 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?		

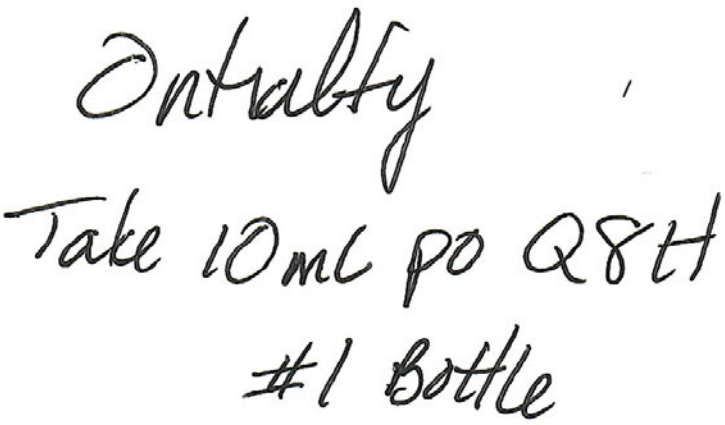
<table>
<tr><th colspan="3">Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).</th></tr>
<tr><td>Step 1</td><td colspan="2">Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to 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. Ontralfy Study (Conducted on 7/5/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order  	Ontralfy Take 10 mL by mouth every 8 hours. Dispense 1 bottle
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Ontralfy	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Ontralfy People Received Study: 194 People Responded: 95					
Total					
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
Total	25	24	21	25	95
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
ANTRALFY	0	0	1	0	1
ANTRELVY	0	0	1	0	1
ATRALFEY	0	0	1	0	1
ATRULFI	0	0	1	0	1
DUTRALFY	1	0	0	0	1
ENDRALFI	0	0	1	0	1
ENTRALFEE	0	0	1	0	1
ENTRALFY	0	0	1	0	1
ODTRALFY	0	0	1	0	1
ONHALFY	0	1	0	0	1
ONTABFY	0	1	0	0	1
ONTALFY	0	1	0	0	1
ONTIALFY	0	3	0	0	3
ONTIALTY	0	1	0	0	1
ONTRABFY	0	3	0	0	3
ONTRABTY	0	1	0	0	1
ONTRAFFY	1	0	0	0	1
ONTRALFEE	0	0	1	0	1
ONTRALFI	0	0	2	0	2
ONTRALFY	18	7	7	24	56
ONTRALTY	0	6	0	0	6
ONTRELFY	0	0	1	0	1
ONTROFI	0	0	1	0	1
ONTROUFY	0	0	1	0	1
ONTRUZANT	0	0	0	1	1
ORTRALFY	1	0	0	0	1
OUTRAFFY	1	0	0	0	1
OUTRALFY	3	0	0	0	3

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

No.	Proposed name: Ontralfy Pronunciation: on tral' fee Established name: tizanidine Dosage form: oral solution Strength(s): 2 mg/5 mL Dosage: 2 mg (5 mL) to 12 mg (30 mL) every 6 hours to 8 hours	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.
	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

No.	Name	POCA Score (%)
	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: Ontralfy Pronunciation: on tral' fee Established name: tizanidine Dosage form: oral solution Strength(s): 2 mg/5 mL Dosage: 2 mg (5 mL) to 12 mg (30 mL) every 6 hours to 8 hours	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.	Ontruzant	58	See FMEA in Section 2.2.4.
2.	(b) (4)***	42	See FMEA in Section 2.2.4.

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

No.	Name	POCA Score (%)
	N/A	

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.	Contrased	58	Veterinary product.

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

No.	Name	POCA Score (%)
	N/A	

[k] 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/

RINA N PATEL
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HINA S MEHTA
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PROPRIETARY NAME REVIEW

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

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

Date of This Review:	August 21, 2023
Application Type and Number:	NDA 216190
Product Name and Strength:	Ontralfy (tizanidine oral solution), 2 mg/5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Fidelity BioPharma Co. (Fidelity)
PNR ID #:	2023-1044725163
DMEPA 2 Safety Evaluator:	Rina Patel, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD
DMEPA 2 Acting Associate Director for Nomenclature and Labeling:	Hina Mehta, PharmD

Contents

1 INTRODUCTION

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

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on May 31, 2023.

- Intended Pronunciation: on tral' fee
- Active Ingredient: tizanidine
- Indication of Use (b) (4) of spasticity
- Route of Administration: oral
- Dosage Form: oral solution
- Strength: 2 mg/5 mL
- Dose and Frequency:
    - Recommended starting dose: 2 mg (5 mL) every 6 to 8 hours up to a maximum of 3 doses in 24 hours.
    - Dosage can be increased by 2 mg (5 mL) to 4 mg (10 mL) per dose, with 1 to 4 days between increases
    - Total daily dose should not exceed 36 mg.
- How Supplied: 473 mL filled into a 16 oz (b) (4) bottle with a CR closure.
- Storage: Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]
- Reference Listed Drugs:
    - Zanaflex (tizanidine hydrochloride) NDA 020397
    - Zanaflex Capsules (tizanidine hydrochloride) NDA 021447

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Ontralfy would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) and the Division of Neurology 1 (DN 1) concurred with the findings of OPDP's assessment for Ontralfy.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

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

We note that the proposed name, Ontralfy, contains the letter string 'TR' which is a modifier intended to mean 'time release'. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of the letter string embedded in the middle of the name is unlikely to be separated from the surrounding letters in a manner that could lead to confusion in this case. Beyond this abbreviation, we note that Ontralfy does not contain any additional components (i.e., route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On June 16, 2023, the Division of Neurology 1 (DN 1) did not forward any comments or concerns relating to Ontralfy at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-seven (87) practitioners participated in DMEPA's prescription studies for Ontralfy. Appendix B contains the results from the prescription simulation studies.

Eight (8) participants misinterpreted the first three letters on Ontralfy to be "Omt" in the inpatient study. We searched commonly used drug databases for potential look-alike or sound-alike names that begin with "Omt" and did not identify any additional names of concern.

One participant in the Computerized Physician Order Entry (CPOE) study selected the proprietary name "Ironmar" from a Dynamic Contains (DC) picklist. Upon further evaluation, we note the participant typed an incorrect sequence of letters ("onma" instead of "ontr"), which resulted in a picklist that did not contain Ontralfy as a choice. Thus, this DC picklist only showed an alphabetically ordered list of names containing the typed letter string of "onma", which was only 1 name (Ironmar). We note 36 seconds elapsed before the participant selected their response from this short picklist, and the participant commented that the name was "Onmalfry or something like that". This suggests that the participant knew the correct name was not listed. Since the simulation software does not allow the participant to go back to the previous page, the participant made a selection to move onto the next part of the study. We determined this study response is unlikely to be representative of a plausible CPOE based risk. We also were unable to

[a] USAN stem search conducted on June 5, 2023.

identify the drug name “Ironmar” in any commonly used drug databases. Therefore, we did not identify concerns with this name pair that could lead to confusion (see Appendix G).
The other 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.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[b] identified 82 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.

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 Prescription 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%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	69
Low similarity name pair: combined match percentage score ≤54%	15

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

Our analysis of the 85 names contained in Table 1 determined none of the names will pose a risk for confusion with Ontralfy as described in Appendices C through H.

2.2.8 Communication of DMEPA’s Determination

On August 21, 2023, DMEPA 2 communicated our determination to the Division of Neurology 1 (DN 1).

3 CONCLUSION

The proposed proprietary name, Ontralfy, is conditionally acceptable.

If you have any questions or need clarifications, please contact Lopa Thambi, OSE project manager, at 301-796-5354.

[b] POCA search conducted on June 7, 2023 in version 5.2.

3.1 COMMENTS TO FIDELITY BIOPHARMA CO.

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

If any of the proposed product characteristics as stated in your submission, received on May 31, 2023, 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. [c]

[c] 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[d]. 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.

[d] 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.			
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.

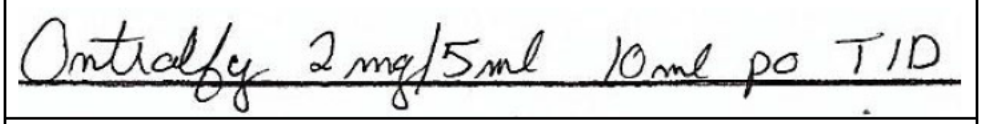
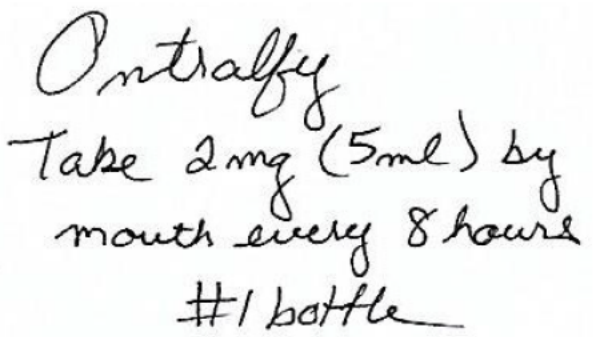
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Ontralfy Study (Conducted on June 9, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Ontralfy 2 mg/5ml 10ml po TID	Ontralfy Take 2 mg or 5 mL by mouth every 8 hours Dispense 1 bottle
Outpatient Prescription:  Ontralfy Take 2mg (5ml) by mouth every 8 hours #1 bottle	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Ontralfy	

FDA Prescription Simulation Responses (Aggregate Report)

As of Date: 07/24/2023 11:56

Study Name: Ontralfy

254 People Received Study

87 People Responded

Total	24	21	22	20	87
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
ANDROUPHY	0	0	1	0	1
ANTRALFI	0	0	3	0	3
ANTRALFY	0	0	1	0	1
ANTRAVFI	0	0	1	0	1
ENTRALFI	0	0	1	0	1
IRONMAR	0	0	0	1	1
OMTIDFLY	1	0	0	0	1
OMTIDFY	4	0	0	0	4
OMTIGFY	1	0	0	0	1
OMTRALFY	2	1	0	0	3
ONTIALFY	3	0	0	0	3
ONTIDFY	6	0	0	0	6
ONTRAFLY	0	1	0	0	1
ONTRALFEE	0	0	3	0	3
ONTRALFI	0	0	4	0	4
ONTRALFY	5	19	4	19	47
ONTRAOFI	0	0	1	0	1
ONTROLFY	2	0	0	0	2
UNTALFY	0	0	1	0	1
UNTRELVY	0	0	1	0	1
UTRIAFEE	0	0	1	0	1

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

No.	**Proposed name:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	**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.	Ontralfy***	100	Name is subject of this review.

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

No.	Name	POCA Score (%)
1.	Lo/Ovral Fe	62
2.	(b) (4)***	58
3.	Atralin	56
4.	Entresto	56
5.	Nitrol	56

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:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	**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.	Bontril	64	This name pair has sufficient orthographic and phonetic differences.
2.	Contraflam	62	Orthographically, the lengths of the names (8 letters vs. 10 letters) are dissimilar when scripted. Furthermore, Ontralfy contains the downstroke letter 'y' in the 8th (last) position which is not present in Contraflam. These differences give the names different shapes when scripted. Phonetically, the first and third syllables ('on' vs. 'kaan' and 'fee' vs. 'flam') sound different when spoken.

No.	**Proposed name:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	**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**
			Additionally, the following differences in product characteristics may help to minimize risk if included on a prescription: • Dosage form: oral solution vs. capsule • Strength: 2 mg/5 mL vs. 250 mg
3.	Contrave	62	Orthographically, Ontralfy contains the upstroke letter 'l', optional downstroke/upstroke letter 'f', and downstroke letter 'y' in the last three positions of the name which are not seen in Contrave. This gives the names different shapes when scripted. Phonetically, the name pair have a different number of syllables (3 vs. 2) that all sound different. Additionally, the following differences in product characteristics may help to minimize risk if included on a prescription: • Dosage form: oral solution vs. extended-release tablet • Strength: 2 mg/5 mL vs. 8 mg/90 mg • Frequency of administration: every 6 to 8 hours vs. once or twice daily
4.	Intrarosa	62	This name pair has sufficient orthographic and phonetic differences.
5.	Nutralox	62	This name pair has sufficient orthographic and phonetic differences.
6.	Anthralin	60	This name pair has sufficient orthographic and phonetic differences.
7.	Control Rx	60	This name pair has sufficient orthographic and phonetic differences.
8.	Nutrilyte	60	This name pair has sufficient orthographic and phonetic differences.
9.	Zantryl	60	Orthographically, the name pair starts with different letters ('O' vs. 'Z') which provides some orthographic difference. Furthermore, Ontralfy contains the downstroke letter 'y' in

No.	**Proposed name:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	**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**
			the last position while Zantryl contains the upstroke letter 'l' in the last position giving the names different shapes when scripted. Phonetically, the name pair have a different number of syllables (3 vs. 2) which sound different when spoken. Additionally, the following differences in product characteristics may help to minimize risk if included on a prescription: • Dosage form: oral solution vs. capsule • Strength: 2 mg/5 mL vs. 37.5 mg • Frequency of administration: every 6 to 8 hours vs. once daily
10.	Intralipid 10%	59	This name pair has sufficient orthographic and phonetic differences.
11.	Intralipid 20%	59	This name pair has sufficient orthographic and phonetic differences.
12.	Intralipid 30%	59	This name pair has sufficient orthographic and phonetic differences.
13.	Andro La 200	58	This name pair has sufficient orthographic and phonetic differences.
14.	Anthrasil	58	This name pair has sufficient orthographic and phonetic differences.
15.	Gonal-F Rff	58	This name pair has sufficient orthographic and phonetic differences.
16.	Integra F	58	This name pair has sufficient orthographic and phonetic differences.
17.	Lidotral	58	This name pair has sufficient orthographic and phonetic differences.
18.	Ontruzant	58	This name pair has sufficient orthographic and phonetic differences.
19.	Trilafon	58	This name pair has sufficient orthographic and phonetic differences.
20.	Gonal-F	57	This name pair has sufficient orthographic and phonetic differences.
21.	Introvale	57	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	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**
22.	Nostrilla	57	This name pair has sufficient orthographic and phonetic differences.
23.	Nutraplus	57	This name pair has sufficient orthographic and phonetic differences.
24.	Atrosulf-1	56	This name pair has sufficient orthographic and phonetic differences.
25.	Bonikraft	56	This name pair has sufficient orthographic and phonetic differences.
26.	Bontril Pdm	56	This name pair has sufficient orthographic and phonetic differences.
27.	Entadfi	56	Orthographically, the name pair starts with different letters (‘O’ vs. ‘E’) which provides some orthographic difference. Furthermore, Ontralfy contains the downstroke letter ‘y’ in the last position while Entadfi contains the dotted letter ‘i’ in the last position giving the names different shapes when scripted. Phonetically, the onset of the first syllables (‘on’ vs. ‘en’) and second syllables (‘tral’ vs. ‘tad’) sound different when spoken. Additionally, the following differences in product characteristics may help to minimize risk if included on a prescription: • Dosage form: oral solution vs. capsule • Frequency of administration: every 6 to 8 hours vs. once daily
28.	Inderal LA	56	This name pair has sufficient orthographic and phonetic differences.
29.	Intron A	56	This name pair has sufficient orthographic and phonetic differences.
30.	Point Relief	56	This name pair has sufficient orthographic and phonetic differences.
31.	Ultralytic 2	56	This name pair has sufficient orthographic and phonetic differences.
32.	Yosprala	56	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Ontralfy **Established name:** tizanidine **Dosage form:** oral solution **Strength(s):** 2 mg/5 mL **Usual Dose:** 2 mg (5 mL) to 12 mg (30 mL)	**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**
33.	Optiray 160	55	This name pair has sufficient orthographic and phonetic differences.
34.	Optiray 240	55	This name pair has sufficient orthographic and phonetic differences.
35.	Optiray 300	55	This name pair has sufficient orthographic and phonetic differences.
36.	Optiray 320	55	This name pair has sufficient orthographic and phonetic differences.
37.	Optiray 350	55	This name pair has sufficient orthographic and phonetic differences.
38.	Onglyza	44	This name pair has sufficient orthographic and phonetic differences.
39.	Onfi	38	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.	Conray	52
2.	Conray 30	52
3.	Conray 43	52
4.	Conray 280	52
5.	Conray 325	52
6.	Conray 400	52
7.	Soolantra	52
8.	Poractant Alfa	50
9.	Thyrotropin Alfa	46

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)***	68	Proposed proprietary name for BLA 761180 found unacceptable by DMEPA (OSE# 2020-39490605-1) dated April 28, 2021. BLA 761180 approved under proprietary name Adbry.

No.	Name	POCA Score (%)	Failure preventions
2.	(b) (4)***	64	Name identified in Names Entered by Safety Evaluator database. (b) (4)*** is a proposed modifier for the proposed proprietary name Crestor (b) (4)*** which is under review for IND 124210. We do not anticipate an order written just for the modifier (b) (4)*** without additional clarification needed. Thus, in this case we do not have a concern with the modifier being confused with this name under review.
3.	(b) (4)***	64	(b) (4)
4.	Vontrol	64	Brand discontinued with no generic equivalents available. NDA 016033 withdrawn FR effective 03/13/2009.
5.	Onkalta***	63	CBER proposed proprietary name for BLA 125593 found unacceptable by CBER on March 9, 2016. The BLA 125593 was withdrawn on November 16, 2016.
6.	Ontayva***	62	Proposed proprietary name for IND 125379 found unacceptable by DMEPA (OSE #2018-26498771 dated January 22, 2019). Corresponding NDA 212608 approved under proprietary name Ayvakit.
7.	Xatral Sr	62	International drug marketed in various countries.
8.	Anturol	61	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
9.	Fortral	61	International drug marketed and formerly marketed in various countries.
10.	Introl	61	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
11.	Antrenyl	60	Brand discontinued with no generic equivalents available. NDA 008492 withdrawn FR effective 06/25/1993. Also, this is an international product marketed in India and formerly marketed in Belgium, Switzerland, and the Netherlands various countries.
12.	Andro La	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
13.	Androxy	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
14.	Antrocol	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.

No.	Name	POCA Score (%)	Failure preventions
15.	Entrocel	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
16.	Infalyte	58	Name identified in RxNorm database. Former name of an oral electrolyte solution, now marketed as Enfamil Enfalyte.
17.	Nitronal	58	Brand discontinued with no generic equivalents available. NDA 018672 withdrawn FR effective 09/13/2000.
18.	Tenotryl	58	Veterinary product.
19.	Xtra-Lax	57	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
20.	Aknetrol	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Drontal	56	Veterinary product.
22.	Metrolyl	56	International product marketed in the United Kingdom.
23.	Tetralysal	56	International product marketed in various countries.
24.	(b) (4)***	56	Proposed proprietary name for BLA 761240 found to be acceptable (OSE# 2021-1044724064); however, the proposed proprietary name was withdrawn by the Applicant on August 29, 2022. BLA 761240 is pending, and the Applicant proposed a new proprietary name, Loqtorzi***, on September 1, 2022. The proposed proprietary name, Loqtorzi***, was found to be acceptable on November 18, 2022 (OSE# 2022-1044724728).
25.	Ultralytic	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
26.	Andryl 200	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
27.	Anthraforte	55	International product formerly marketed in Canada.
28.	Nafronyl	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
29.	Tanoral	52	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
30.	Lynoral	50	Product is discontinued with no generics available in the US. International product marketed in Indonesia and India.

No.	Name	POCA Score (%)	Failure preventions
31.	Ironmar	34	Name identified in FDA Simulation Study. Unable to find product characteristics in commonly used drug databases.

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

No.	Name	POCA Score (%)
	N/A	

[e] 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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