CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217006Orig1s000

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:	February 3, 2023
Application Type and Number:	NDA 217006
Product Name and Strengths:	Abilify Asimtufii (aripiprazole) extended-release injectable suspension, 720 mg/2.4 mL and 960 mg/3.2 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Otsuka Pharmaceutical Company, Ltd. (Otsuka)
PNR ID #:	2022-1044724837
DMEPA 1 Safety Evaluator:	Loretta Holmes, BSN, PharmD
Acting DMEPA 1 Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Abilify Asimtufii, 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. Otsuka submitted an external name study, conducted by [redacted] (b) (4) for this proposed proprietary name.

1.1 REGULATORY HISTORY

Otsuka currently markets three aripiprazole drug formulations:

- Abilify (aripiprazole) tablets, NDA 021436 (approved on 11/15/2002)
- Abilify Maintena (aripiprazole) for extended-release injectable suspension, NDA 202971 (approved on 02/28/2013)
- Abilify MyCite (aripiprazole tablets with sensor), NDA 207202 (approved on 11/13/2017)

On January 26, 2022 Otsuka submitted the proposed proprietary name, [redacted] (b) (4) ***, under IND 134612, for review as an extension of their aripiprazole containing products under the family tradename, Abilify. On August 16, 2022 the proposed proprietary name, [redacted] (b) (4) ***, was submitted for review under NDA 217006. DMEPA 1 met with Otsuka via teleconference on October 28, 2022 to discuss our preliminary concerns with the proposed name.[a] Thus, on November 9, 2022, Otsuka withdrew the proposed proprietary name, [redacted] (b) (4) *** under IND 134612 and NDA 217006, and submitted the name, Abilify Asimtufii, for review under NDA 217006.

1.2 PRODUCT INFORMATION

The following Abilify Asimtufii product information is provided in the proprietary name submission received on November 9, 2022. Product information for Abilify MyCite, Abilify Maintena, and Abilify is also provided in Table 1, below.[b]

Table 1. Relevant Product Information for Abilify Asimtufii, Abilify MyCite, Abilify Maintena, and Abilify

	Abilify Asimtufii (proposed product)	Abilify MyCite	Abilify Maintena	Abilify
Initial Approval Date	N/A	11/13/2017	02/28/2013	11/15/2002
Active Ingredient	aripiprazole	aripiprazole	aripiprazole	aripiprazole
Proposed Pronunciation	a bil' i fye ah-sim-tuh-fye	a BIL ĭ fī Mi SIHYT	a-BIL-i-fy main-TEN-a	a BIL ĭ fī

[a] Nguyen, P. Teleconference Meeting Minutes—[redacted] (b) (4). Silver Spring (MD): FDA, CDER, OSE, OMEPRM, DMEPA 1 (US); 2022 October 28. NDA 217006.

[b] Abilify MyCite, Abilify Maintena, and Abilify [Prescribing Information] DailyMed. U.S. National Library of Medicine. [cited 2023 Jan 24]. Available from: DailyMed - FDA Resources: SPL, Other Prescription Drug Labeling Resources, and Guidances (nih.gov).

Table 1. Relevant Product Information for Abilify Asimtufii, Abilify MyCite, Abilify Maintena, and Abilify				
	Abilify Asimtufii (proposed product)	**Abilify MyCite**	**Abilify Maintena**	**Abilify**
Indication	• Treatment of schizophrenia in adults • Maintenance monotherapy treatment of bipolar I disorder in adults	Abilify MyCite, a drug-device combination product comprised of aripiprazole tablets embedded with an Ingestible Event Marker (IEM) sensor intended to track drug ingestion, is indicated for the: • Treatment of adults with schizophrenia. • Treatment of bipolar I disorder o Acute treatment of adults with manic and mixed episodes as monotherapy and as adjunct to lithium or valproate. o Maintenance treatment of adults as monotherapy and as adjunct to lithium or valproate. • Adjunctive treatment of adults with Major Depressive Disorder.	• Treatment of schizophrenia in adults • Maintenance monotherapy treatment of bipolar I disorder in adults	• Schizophrenia • Acute Treatment of Manic and Mixed Episodes associated with Bipolar I • Adjunctive Treatment of Major Depressive Disorder • Irritability Associated with Autistic Disorder • Treatment of Tourette's disorder
Route of Administration	Gluteal intramuscular injection	Oral	Deltoid or gluteal intramuscular injection	Oral
Dosage Form	Extended-release injectable suspension	Tablets with sensor	For extended-release injectable suspension	Tablet
Strengths	720 mg/2.4 mL and 960 mg/3.2 mL	2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg	300 mg and 400 mg	2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg
Dose and Frequency	960 mg administered once every two months as a single	(abbreviated): The dosage range is 2 mg to 30 mg once daily,	Recommended starting and maintenance dose is 400 mg administered	(abbreviated): The dosage range is 2 mg to 30 mg

Table 1. Relevant Product Information for Abilify Asimtufii, Abilify MyCite, Abilify Maintena, and Abilify				
	Abilify Asimtufii (proposed product)	**Abilify MyCite**	**Abilify Maintena**	**Abilify**
	injection. Dose can be reduced to 720 mg in patients with adverse reactions. (There are recommended dosage adjustments for patients taking CYP2D6 inhibitors, CYP3A4 inhibitors, or CYP3A4 inducers for greater than 14 days.)	depending upon the indication. (Dosage adjustments are recommended in patients who are known CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors or strong CYP3A4 inducers.)	monthly as a single injection. Dose can be reduced to 300 mg in patients with adverse reactions. (There are recommended dosage adjustments for patients taking CYP2D6 inhibitors, CYP3A4 inhibitors, or CYP3A4 inducers for greater than 14 days.)	once daily, depending upon the indication. (Dosage adjustments are recommended in patients who are known CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors or strong CYP3A4 inducers.)
How Supplied	Single-use kit containing 1 pre-filled syringe and 2 safety needles (a 1.5 inch 22 gauge needle and a 2 inch 21 gauge needle).	1-component patch: Kit containing bottle of 30 tablets with sensor +7 MyCite patches 2-component patch: *30-day starter kit*: Bottle of 30 tablets with sensor + 1 MyCite pod and 7 MyCite strips *Maintenance kit*: Bottle of 30 tablets with sensor + 7 MyCite strips	Pre-filled Dual Chamber Syringe: Kit containing a single-dose, pre-filled, dual chamber syringe containing Abilify Maintena (aripiprazole) for extended-release injectable suspension lyophilized powder and Sterile Water for Injection One 23-gauge, 1-inch safety needle One 22-gauge, 1.5-inch safety needle One 21-gauge, 2-inch safety needle Single-Use Vial: Kit containing a single-use vial of Abilify Maintena (aripiprazole) extended-release injectable suspension lyophilized powder 5-mL, single-use vial of Sterile Water for Injection, USP One 3-mL, luer lock syringe with pre-attached 21-gauge, 1.5-inch safety needle One 3-mL, luer lock disposable syringe with luer lock tip	2 mg: Bottle of 30 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg: Bottle of 30; Blister of 100

Table 1. Relevant Product Information for Abilify Asimtufii, Abilify MyCite, Abilify Maintena, and Abilify				
	Abilify Asimtufii (proposed product)	**Abilify MyCite**	**Abilify Maintena**	**Abilify**
			One vial adapter One 23-gauge, 1-inch safety needle One 22-gauge, 1.5-inch safety needle One 21-gauge, 2-inch safety needle	
Storage	Store at 25°C (77°F), excursions permitted between 15° and 30°C (59° to 86°F) [see USP Controlled Room Temperature].	Tablet bottle: Store 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Do not store in conditions where tablets are exposed to humid conditions. MyCite Patch (Wearable Sensor): Store between 5°C and 27°C (41°F to 81°F), 15% to 93% relative humidity.	Pre-filled dual chamber syringe: Store below 30°C [86°F]. Do not freeze. Protect the syringe from light by storing in the original package until time of use. Vial: Store at 25°C (77°F), excursions permitted between 15°C and 30°C (59°F to 86°F) [see USP Controlled Room Temperature].	Store at 25°C (77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Abilify Asimtufii 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 Abilify Asimtufii. The Division of Psychiatry (DP) did not comment on the findings of OPDP's assessment for Abilify Asimtufii.

2.2 SAFETY ASSESSMENT

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

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

This proprietary name is comprised of the root name "Abilify" and the modifier "Asimtufii". Otsuka indicated in their submission that the proposed proprietary name, Abilify Asimtufii, has the following derivation: "Abilify is an FDA approved proprietary name. Asimtufii is intended to imply how bimonthly dosing simplifies therapy." Otsuka did not provide the intended meaning of the modifier, stating "not applicable". The use of the modifier, Asimtufii, is discussed in Section 2.2.5.

The modifier, Asimtufii, contains the medical abbreviation "As" (left ear) at the beginning and the abbreviations "im" (intramuscular) and "mt" (micro tablet) in the middle. We typically discourage the inclusion of medical abbreviations in proprietary names. However, considering that the beginning letters "As" are a medical abbreviation, we evaluated the potential risk of misinterpreting the proposed modifier, Asimtufii, as "As [drug name Imtufii]" and did not identify any names of concern.[d] Additionally, we determined that due to the location of the abbreviations "im" and "mt" in the middle of the name and their lack of prominence, they are unlikely to be separated from the surrounding letters in a manner that could lead to confusion. Furthermore, because Asimtufii is a modifier, the root name Abilify would likely precede it on a prescription which would provide an additional measure of safety.

2.2.3 Comments from Other Review Disciplines at Initial Review

On December 23, 2022, the Division of Psychiatry (DP) did not forward any comments or concerns relating to Abilify Asimtufii at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred two (102) practitioners participated in DMEPA's prescription studies for Abilify Asimtufii. Three participants in the FDA Name Simulation Studies [inpatient written (n=1) and voice (n=2)], omitted the proposed modifier, Asimtufii. We acknowledge that omission and oversight of a modifier is cited in literature as a common cause of medication errors.[e] However, when used, modifiers can assist in conveying certain aspects of the product characteristics and provide additional measures to differentiate between products. We evaluate the use of the same root name Abilify and a modifier to differentiate the product in Section 2.2.5.

One participant in the Computerized Physician Order Entry (CPOE) portion of the FDA Name Simulation Studies entered "abilify" and selected "Abilify Maintena Kit" from the dropdown menu. We recognize that because Abilify Maintena and Abilify Asimtufii share the same root name, the potential exists for product selection errors to occur from a CPOE dropdown menu. This is not a unique occurrence with products that share the same root name. However, Abilify

[c] USAN stem search conducted on January 9, 2023.

[d] POCA search for "imtufii" conducted on January 31, 2023 in version 5.2.

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

Maintena and Abilify Asimtufii differ in strength, dose, and frequency of administration (see Table 1) which may provide an added measure of safety.

One participant in the written inpatient portion of the FDA Name Simulation Studies interpreted the name as "Abilify Aristada". Aristada is the name of a currently marketed long-acting injectable aripiprazole lauroxil product. We note that the participant also interpreted another proposed name in the study as a currently marketed product, so it is unclear whether the participant was intentionally trying to provide the names of currently marketed products. We note that it is unlikely that the name, Abilify, would be used as a root name in conjunction with the name Aristada as a modifier.

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 Safety Assessment of the Proposed Modifier

In this section, we provide a safety analysis of the proposed proprietary name, Abilify Asimtufii. Otsuka currently markets the active ingredient, aripiprazole, under the following family of products: Abilify (aripiprazole) tablets, Abilify Maintena (aripiprazole) for extended-release injectable suspension, and Abilify MyCite (aripiprazole tablets with sensor). Otsuka proposes to differentiate their proposed injection, administered every 2-months, from their currently marketed products by using the proposed modifier, Asimtufii. Differences between the proposed product and the currently marketed products are listed in Table 1.

Given Otsuka's proposal to use Abilify as the root name with the addition of a modifier, we evaluated the following (addressed respectively below): 1) use of the same root name, 2) use of a modifier to differentiate the product, and 3) the proposed modifier, Asimtufii.

1. **Evaluation of the use of the same root name "Abilify"**
   The use of the root name, Abilify, conveys that Abilify Asimtufii is a family product line extension. We note that the proposed product contains the same active ingredient as the other currently marketed products in the family product line. Our routine postmarketing surveillance has not identified the root name, Abilify, as a source of name confusion and medication errors.[f] Therefore, we do not object to the use of the root name, Abilify, in the proposed proprietary name, Abilify Asimtufii.

2. **Evaluation of the use of a modifier to differentiate the product**

   Otsuka's aripiprazole product line consists of Abilify, Abilify Maintena, and Abilify MyCite. Otsuka proposes to differentiate this product from the existing products by using the modifier, Asimtufii. The names Abilify Maintena and Abilify MyCite contain modifiers as part of the proprietary name to help distinguish these products from Abilify. We note that Abilify is a tablet, Abilify MyCite is a tablet with sensor, Abilify Maintena is a for extended-

[f] Holmes, L. Proprietary Name Review for Abilify Maintena (NDA 202971). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2012 May 21. OSE RCM # 2012-492.

release injectable suspension administered once monthly, and Abilify Asimtufii is an extended-release injectable suspension administered once every two months. Therefore, the addition of a modifier to the root name, Abilify, may help to differentiate Abilify Asimtufii from the currently marketed Abilify products. See Table 1 for additional comparison of product characteristics between Abilify, Abilify Maintena, Ability MyCite and the proposed Abilify Asimtufii.

In our evaluation, we considered the risk of name confusion if the modifier is omitted or overlooked, as seen in the FDA Prescription Simulation Study. In the FDA Prescription Simulation Study, three participants in the FDA Name Simulation Studies [inpatient written (n=1) and voice (n=2)], omitted the proposed modifier, Asimtufii. We note that omission and oversight of a modifier is cited in literature as a common cause of medication errors.[g] Postmarketing experience shows that the introduction of product line extensions may result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. In this case, if the modifier is dropped or overlooked or not heard, it is unlikely that Abilify would get dispensed because of the multiple product characteristic differences between Abilify and Abilify Asimtufii [e.g., strengths (2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg *versus* 720 mg/2.4 mL and 960 mg/3.2 mL), dose (2 mg to 30 mg *versus* 720 mg or 960 mg), route of administration (oral *versus* intramuscular injection), and frequency of administration (once daily *versus* once every 2 months)], which when written on a prescription or verbally stated, may provide an added measure of safety.

Although the proposed naming strategy is not devoid of risk because modifiers may be omitted, modifiers can assist in differentiating products and may help to prevent potential selection errors when used. An alternative to using a modifier to distinguish Abilify Asimtufii from the currently marketed Abilify products is to use a different proprietary name (i.e., one that does not use the root name Abilify). However, marketing the new product under a unique proprietary name also carries a risk of medication errors, including the potential for patients to be inadvertently placed on multiple aripiprazole products (therapeutic duplication) if the proprietary names are not recognized as having the same active ingredient. This may lead to overdose and adverse drug events. These errors may have greater associated safety risks than the omission or oversight of the modifier as discussed above. Thus, based on the totality of this information, we do not object to the use of a modifier for this product as it may provide an added measure of safety.

3. Evaluation of the proposed modifier "Asimtufii"

According to Otsuka, the derivation of the modifier "Asimtufii" is that it "is intended to imply how bimonthly dosing simplifies therapy". Regarding the meaning of the modifier, Otsuka stated, "not applicable". We note that the modifier, Asimtufii, is novel and has no well understood standard meaning in drug nomenclature. However, it is reasonable to expect that, like any novel modifier, awareness among healthcare practitioners will increase with market uptake of the product. According to the external name study conducted by (b) (4) one of the factors assessed was whether Asimtufii is "well suited as a modifier to

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

communicate q2Mo administration" and for 160/180 (89%) of responses, the findings and comments were that "this modifier clearly differentiates this formulation".

We again note that one participant in the inpatient portion of the FDA Name Simulation Studies interpreted the name as "Abilify Aristada" (see Section 2.2.4). It is unlikely that the name, Abilify, would be used as a root name in conjunction with the name Aristada as a modifier. Additionally, Abilify Asimtufii and Aristada differ in strength and dose (720 mg/2.4 mL and 960 mg/3.2 mL *versus* 441 mg/1.6 mL, 662 mg/2.4 mL, 882 mg/3.2 mL, and 1064 mg/3.9 mL), which provides an added measure of safety. Therefore, we do not object to the use of the modifier, Asimtufii, for this proposed product.

In summary, we find the use of the root name "Abilify" acceptable for the product and we find that the addition of the proposed modifier "Asimtufii" to the root name may provide an additional layer of safety in differentiating the proposed product from the currently marketed Abilify, Abilify Maintena, and Ability MyCite. Although the naming strategy presents some risk of product selection error if the modifier is dropped, overlooked, or not heard, we find the residual risk acceptable. Therefore, based on the totality of information considered above, we do not object to the proposed proprietary name, Abilify Asimtufii for NDA 217006.

2.2.6 Communication of DMEPA's Determination

On February 3, 2023, DMEPA 1 communicated our determination to the Division of Psychiatry (DP).

3 CONCLUSION

The proposed proprietary name, Abilify Asimtufii, is conditionally acceptable.

If you have any questions or need clarifications, please contact Phuong B. Nguyen, OSE Safety Regulatory Project Manager, at 240-402-5827.

3.1 COMMENTS TO OTSUKA PHARMACEUTICAL COMPANY, LTD.

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

If any of the proposed product characteristics as stated in your submission, received on November 9, 2022 are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

APPEARS THIS WAY ON ORIGINAL

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. [h]

***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)).

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

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[i]. 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 are 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.

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,

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

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	**Y/N**	Do the syllables have different phonologic processes, such

	a different number or placement of upstroke/downstroke letters present in the names?		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.

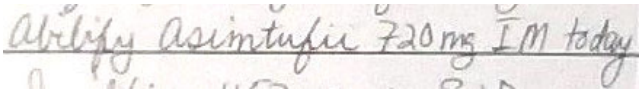
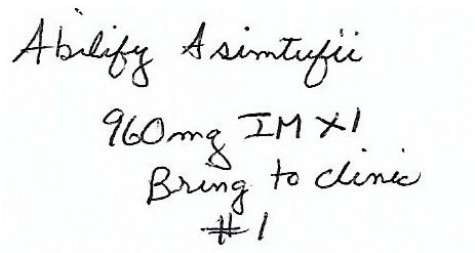
<table>
<tr><td></td><td colspan="2">• Similar sounding doses: 15 mg is similar in sound to 50 mg</td></tr>
<tr><td rowspan="2">Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</td></tr>
<tr><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 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?</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: 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. Abilify Asimtufii Study (Conducted on November 28, 2022)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Abilify Asimtufii 960 mg IM one time Bring to clinic Dispense 1
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Abilify Asimtufii	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Abilify Asimtufii					
262 People Received Study					
102 People Responded					
Total	26	23	25	28	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
ABILIFY	1	0	2	1	4
ABILIFY ACEMPTIFY	0	0	1	0	1
ABILIFY ARISTADA	1	0	0	0	1
ABILIFY ASEMPTUFY	0	0	2	0	2
ABILIFY ASIMPTOFI	0	0	1	0	1
ABILIFY ASIMPTOFY	0	0	1	0	1
ABILIFY ASIMPTUFI	0	0	1	0	1
ABILIFY ASIMTRUFY	0	0	1	0	1
ABILIFY ASIMTUFFI	0	0	0	1	1
ABILIFY ASIMTUFI	0	0	0	1	1
ABILIFY ASIMTUFIC	1	0	0	0	1

ABILIFY ASIMTUFII	5	22	0	23	50
ABILIFY ASIMTUFIR	9	0	0	0	9
ABILIFY ASINTUFII	3	0	0	1	4
ABILIFY ASINTUFIR	5	0	0	0	5
ABILIFY ASYMPTOFY	0	0	4	0	4
ABILIFY ASYMPTUFY	0	0	4	0	4
ABILIFY ASYMTIFY	0	0	1	0	1
ABILIFY ASYMTOFY	0	0	1	0	1
ABILIFY ASYNCTIFY	0	0	1	0	1
ABILIFY AZEMTIFY	0	0	1	0	1
ABILIFY ISYMPTUFY	0	0	1	0	1
ABILIFY MAINTENA KIT	0	1	0	0	1
ABILIFY/ASYMTUFY	0	0	1	0	1
ABILIFY/OSEMTUFY	0	0	1	0	1
ABILIGY ASIMTUFIR	1	0	0	0	1
ABILITY ASIMTUFII	0	0	0	1	1
ABOLIVIE/ASTIMTIFIE 900 MG IM	0	0	1	0	1

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/

LORETTA HOLMES
02/03/2023 06:39:46 PM

MADHURI R PATEL
02/03/2023 06:46:05 PM

MISHALE P MISTRY
02/07/2023 10:46:10 AM