CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213801Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
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 5, 2021
Application Type and Number:	NDA 213801
Product Name and Strength:	Myrbetriq Granules (mirabegron for Oral Suspension), 8 mg/mL after reconstitution[a]
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Astellas Pharma Global Development, Inc. (Astellas)
Panorama #:	2020-43140108
DMEPA Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA Team Leader (Acting):	Celeste Karpow, PharmD, MPH

[a] Each bottle contains 8.3 g of granules equivalent to 830 mg mirabegron prior to reconstitution.

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Myrbetriq Granules, 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. Astellas did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Myrbetriq (mirabegron) Extended-release tablets, 25 mg and 50 mg was approved under NDA 202611 on June 28, 2012 and is currently approved for the treatment of overactive bladder (OAB) in adults.

The Applicant proposes to expand the Myrbetriq product line to include a new dosage form, mirabegron (8 mg/mL) granules for oral suspension for the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older.

The Applicant previously submitted the proposed proprietary name, Myrbetriq (b) (4) Granules under NDA 213801 for review on September 29, 2020. On December 18, 2020 we submitted an information request (IR) requesting the Applicant provide additional information or rationale to support the use of two modifiers (b) (4) and 'Granules' as part of the Sponsor's proposed proprietary name.[b] In response to our information request, the Applicant submitted a Proprietary Name Review amendment on December 22, 2020[c] to amend the proposed proprietary name to Myrbetriq Granules (i.e., to include only one modifier) which is the subject of this review.

In parallel, Astellas has submitted efficacy supplement (017) under NDA 202611 proposing the addition of the same pediatric indication (treatment of neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older) for the extended-release tablet dosage form.

1.2 PRODUCT INFORMATION

Table 1. Relevant Product Information[d] for Myrbetriq Granules and Myrbetriq

Product Name	Myrbetriq Granules	Myrbetriq
Intended Pronunciation	meer-BEH-trick	meer-BEH-trick
Application #	NDA 213801	NDA 202611

[b] Information request available in DARRTS via: https://darrts fda.gov/darrts/faces/ViewDocument?documentId=090140af805bce25&_afrRedirect=995617049672564

[c] PNR Amendment available in docuBridge via: \\CDSESUB1\evsprod\nda213801\0013\m1\us\1-12-4-proprietary-name-request-amendment.pdf

[d] Prescribing Information labeling proposed under NDA 213801 and NDA 202611/S-017 available in EDR via: \\CDSESUB1\evsprod\nda213801\0001\m1\us\myrbetriq-uspi-redline.doc

Initial Approval Date	N/A	June 28, 2012
Active Ingredient	Mirabegron	Mirabegron
Indication[e]	For the treatment of neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older.	For the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency. In combination with the muscarinic antagonist solifenacin succinate, is indicated for the treatment of OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency.
Route of Administration	Oral	Oral
Dosage Form	for Oral Suspension	Extended-release tablet
Strength	Each bottle contains 8.3 g of granules equivalent to 830 mg mirabegron prior to reconstitution. 8 mg/mL after reconstitution	25 mg and 50 mg
Dose and Frequency[e]	OAB Indication: N/A	OAB Indication: • Recommended starting dose is 25 mg once daily, alone or in combination with solifenacin succinate 5 mg, once daily. • Based on individual efficacy and tolerability, may increase dose to 50 mg once daily, alone or in combination with solifenacin succinate 5 mg, once daily. • Patients with Severe Renal Impairment or Patients with Moderate Hepatic Impairment: Maximum dose is 25 mg MYRBETRIQ once daily • Patients with End Stage Renal Disease (ESRD) or Patients with

[e] NDA 202611/S-017 proposes to expand the indication of Myrbetriq extended-release tablets to include treatment of NDO in pediatric patients aged 3 years and older. S-017 is currently under review by the Agency.

<table>
<tr><td></td><td></td><td>Severe Hepatic Impairment: Not recommended.</td></tr>
<tr><td></td><td colspan="2">NDO Indication:

Myrbetriq Granules for Oral Suspension Monotherapy for Pediatric Patients < 35 kg or ≥ 35 kg:

The recommended starting dose of MYRBETRIQ Granules is determined based on patient weight (refer to Table 1). Dosing should be initiated at the recommended starting dose. Dosage may be titrated to the lowest effective dose but should not exceed the maximum recommended dose.

Table 1: Once Daily Recommended Oral Suspension Dose According to Patient Body Weight
<table>
<tr><th>Recommended Dose</th><th>Body Weight Range</th><th>Tablet Dose</th><th>Suspension Volume[1]</th></tr>
<tr><td rowspan="3">Recommended Starting Dose</td><td>11 kg to less than 22 kg</td><td>--</td><td>3 mL</td></tr>
<tr><td>22 kg to less than 35 kg</td><td>--</td><td>4 mL</td></tr>
<tr><td>greater than or equal to 35 kg</td><td>25 mg</td><td>6 mL[2]</td></tr>
<tr><td rowspan="3">Recommended Maximum Dose</td><td>11 kg to less than 22 kg</td><td>--</td><td>6 mL</td></tr>
<tr><td>22 kg to less than 35 kg</td><td>--</td><td>8 mL</td></tr>
<tr><td>greater than or equal to 35 kg</td><td>50 mg</td><td>10 mL[2]</td></tr>
</table>
--: not applicable; NDO: neurogenic detrusor overactivity.
1. MYRBETRIQ Granules for oral suspension formulation (granules were reconstituted with water to prepare a suspension with a concentration of 8 mg/mL suspension).
2. Patients ≥ 35 kg who cannot swallow tablets may take a suspension dose.
• The oral suspension and extended-release tablet are not bioequivalent; the doses in the table account for the difference in bioavailability between the two formulations.</td></tr>
<tr><td>How Supplied</td><td>Supplied as granules in bottles with a child-resistant cap packaged in an aluminum pouch with desiccant.

Each bottle is reconstituted by the pharmacy with 100 mL (b) (4) water.</td><td>oval, film-coated, extended-release tablets available as:

Bottle of 30 count; bottle of 90 count, (b) (4) .</td></tr>
<tr><td>Storage</td><td>Store at 20°C to 25°C (68°F to 77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Reconstituted oral suspension can be stored at room temperature (b) (4) (b) (4) for up to 28 days</td><td>Store at 25°C (77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F) {see USP controlled Room Temperature}.</td></tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Myrbetriq Granules would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Urology, Obstetrics, and Gynecology (DUOG) concurred with the findings of OPDP's assessment for Myrbetriq Granules.

2.2 SAFETY ASSESSMENT

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

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

The proposed proprietary name, Myrbetriq Granules, is comprised of two components: (1) the root name 'Myrbetriq' and (2) the modifier 'Granules'. The Applicant indicates that the modifier "Granules" is intended to mean 'Granules that need to be reconstituted with water to create an oral suspension.'

The product with the root name Myrbetriq was approved on June 28, 2012 and is currently marketed as an Extended-release tablet. The applicant proposes to add a for oral suspension formulation to the currently marketed Myrbetriq product line. Therefore, we have evaluated the appropriateness of using the same root name and the appropriateness of the proposed modifier 'Granules' in Section 2.2.5 below.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 15, 2020 e-mail, the Division of Urology, Obstetrics, and Gynecology (DUOG) forwarded the following comment relating to Myrbetriq Granules at the initial phase of the review: The word "Granules" in the tradename could imply use as "sprinkles" on soft foods.

We address this comment in Section 2.2.5 Safety assessment of the modifier "Granules."

2.2.4 FDA Name Simulation Studies

Seventy-one practitioners participated in DMEPA's prescription studies for Myrbetriq Granules. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

Five participants (Voice n=4 and CPOE n=1) in the FDA name simulation studies omitted the modifier "Granules." We discuss the risk associated with omission of the modifier, granules in Section 2.2.5 below.

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[f] USAN stem search conducted on November 23, 2020.

Appendix B contains the results from the prescription simulation studies.

2.2.5 Safety Assessment of the Root Name and Modifier, Granules

The applicant currently markets the active ingredient, mirabegron, under the name, Myrbetriq, for the Extended-release tablet formulation. The product is currently approved as 25 mg and 50 mg oral Extended-release tablets for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency. For their proposed mirabegron for oral suspension, the applicant proposes to use the name, Myrbetriq Granules. The differences between the proposed formulation and the currently marketed formulation are listed in Table 1 under Section 1.2 of our review.

1. Evaluation of use of the same root name, "Myrbetriq"

Myrbetriq has been marketed as the proprietary name for mirabegron since approval on June 28, 2012. We note that Myrbetriq and Myrbetriq Granules*** share the same active ingredient and route of administration. Our routine postmarketing surveillance has not identified any signals attributed to name confusion involving Myrbetriq. Thus, we do not object to the use of the root name, Myrbetriq, for this product.

2. Evaluation of the use of the modifier to differentiate the products

Myrbetriq Granules is the second product proposed by the Applicant for the currently marketed Myrbetriq product line. The proposed product represents a new strength (8 mg/mL after reconstitution[g] vs. 25 mg and 50 mg) and new dosage form (for oral suspension vs. Extended-release tablet). Thus, the Applicant proposes to use the modifier "Granules" to distinguish the proposed Myrbetriq Granules product from the currently marketed Myrbetriq product. We evaluated the use of the modifier to determine if the naming strategy helps to distinguish the proposed Myrbetriq Granules product from the currently marketed Myrbetriq product.

It is not uncommon to use modifiers to denote a specific product formulation as part of a product line extension. We note the for oral suspension and Extended-release tablet dosage forms are not bioequivalent on a mg per mg basis. The addition of a modifier may signal to healthcare practitioners that this product differs from the currently marketed Myrbetriq Extended-release tablets, which may help differentiate the products and reduce the potential for wrong dosage form medication errors.

We also considered the risk of name confusion if the modifier is dropped. We note that omission and oversight of a modifier is cited in literature as a common cause of medication errors.[h] 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, there is no direct overlap in strength (8 mg/mL after

[g] Each bottle contains 8.3 g of granules equivalent to 830 mg mirabegron prior to reconstitution.

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

reconstitution[i] vs. 25 mg and 50 mg) or dose (24 mg [3 mL], 32 mg [4 mL], 48 mg [6 mL], 64 mg [8 mL], 80 mg [10 mL] vs. 25 mg or 50 mg) between Myrbetriq Granules and Myrbetriq. As such, other components of the prescription or medication order (e.g., strength, dose, dosage form) would help mitigate the risk of wrong dosage form medication errors if the modifier is omitted on a prescription or medication order.

Although modifiers may be omitted, they can assist in differentiating products and may help to prevent potential selection errors when used. 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. Furthermore, label and labeling mitigations can help minimize the residual risk of product selection errors.

3. Evaluation of the proposed modifier, "Granules"

The Applicant indicates that the modifier "Granules" is intended to mean 'Granules that need to be reconstituted with water to create an oral suspension.' We note that the modifier "Granules" is consistent with the product formulation (pre-reconstitution). We find that the proposed modifier, Granules, is not a medical abbreviation[j], is not a USAN Stem[k], is not on ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations[l], and does not appear to present any overt safety concerns from a look-alike or sound-alike perspective.

At the initial phase of the review, the Division of Urology, Obstetrics, and Gynecology (DUOG) expressed concern that the word "Granules" in the tradename could imply use as "sprinkles" on soft foods (see section 2.2.3 above). As proposed, the use of the modifier "Granules" is inconsistent with USP Nomenclature Guidelines[m] that reserve "Granules" for instances where the drug product is administered as granules (e.g., Singular (montelukast sodium) oral granules that are sprinkled directly in the mouth or in food or liquid). We assessed the risk of Myrbetriq Granules being administered without reconstitution. The proposed product is intended to be dispensed as an oral suspension (i.e., granules reconstituted by the pharmacy before being dispensed to patient/caregiver) and not in its native form (i.e., granules), which would eliminate the risk of wrong technique administration errors (i.e., administering the granules). Additionally, optimized labels and labeling can help mitigate the risk of dispensing and administration errors to an acceptable level.

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[i] Each bottle contains 8.3 g of granules equivalent to 830 mg mirabegron prior to reconstitution.

[j] Davis, N. Medical Abbreviations 30,000 Conveniences at the Expense of Communication and Safety. 14th ed. Warminster, PA; 2009.

[k] USAN stem search conducted on November 23, 2020.

[l] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2017 [cited 2020 NOV 18]. Available from: https://www.ismp.org/recommendations/error-prone-abbreviations-list

[m] Available from USP website (http://www.usp.org/health-quality-safety/compendial-nomenclature); USP Nomenclature Guidelines, referenced in USP General Chapter <1121> Nomenclature, Revised March 24, 2016, p. 36.

As part of our evaluation of the appropriateness of the modifier 'Granules', we reviewed other products which use 'Granules' as part of their proprietary name. The modifier 'Granules' is not new and is currently utilized in the marketplace. We identified one marketed product "Prograf Granules" with the modifier "Granules." Prograf Granules is tacrolimus for oral suspension, 0.2 mg and 1 mg and was approved under NDA 210115 on May 24, 2018 for the prevention of rejection in pediatric heart, kidney, or liver transplant recipients. The proposed dosage form nomenclature (mirabegron for oral suspension) is the same as that used for the marketed Prograf Granules (tacrolimus for oral suspension) product. We note that Prograf Granules also require reconstitution prior to administration and the product labeling contains the instructions "Do not sprinkle Prograf Granules on food". Therefore, there is precedent in the market place for use of the proposed modifier "Granules" consistent with the sponsor's intended meaning for the proposed product. Furthermore, based on our postmarketing surveillance activities, we are not aware of any medication error concerns stemming from the use of the modifier Granules.

Therefore, we do not object to the use of modifier 'Granules' for the proposed product and find Granules is acceptable for conveying this characteristic of the product formulation.

In summary, we find the use of the root name, Myrbetriq, acceptable for the proposed product. Additionally, we find that the addition of the modifier "Granules" to the root name may provide a layer of safety to help differentiate the proposed oral suspension from the currently marketed Extended-release tablet. Furthermore, optimized labels and labeling may be developed to convey the appropriate preparation instructions for the product. Therefore, based on the totality of information considered above, we do not object to the proposed name, Myrbetriq Granules, for the proposed product.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Urology, Obstetrics, and Gynecology (DUOG) via e-mail on February 2, 2021. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Urology, Obstetrics, and Gynecology (DUOG) on February 5, 2021, they stated no additional concerns with the proposed proprietary name, Myrbetriq Granules.

3 CONCLUSION

The proposed proprietary name, Myrbetriq Granules, is acceptable.

If you have any questions or need clarifications, please contact Oyinlola Fashina, OSE project manager, at 301-796-4446.

3.1 COMMENTS TO ASTELLAS PHARMA GLOBAL DEVELOPMENT, INC.

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

If any of the proposed product characteristics as stated in your submission, received on December 22, 2020, 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. [n]

[n] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

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

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

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

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

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

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[o]. 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.

[o] 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. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed 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.

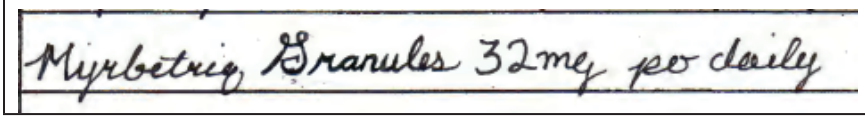
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length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

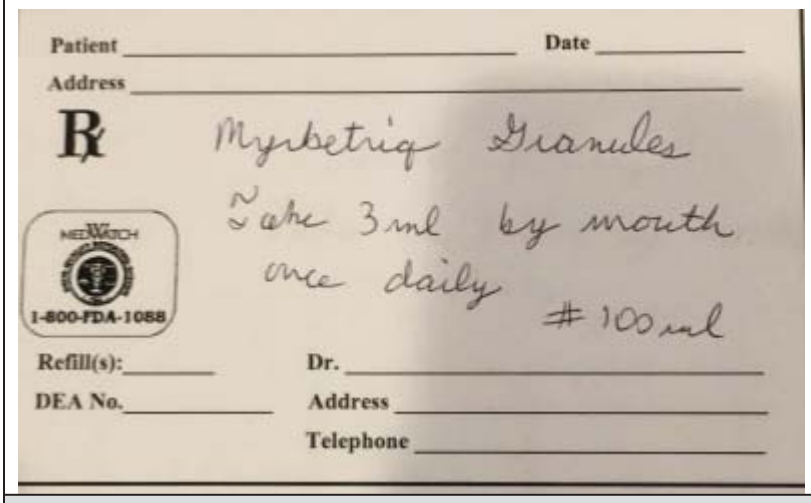
Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

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. Myrbetriq Granules Study (Conducted on January 5, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Myrbetriq Granules Take 3 mL by

Outpatient Prescription:  Patient _____ Date _____ Address _____ ℞ Myrbetriq Granules Take 3 ml by mouth once daily # 100 ml 1-800-FDA-1088 Refill(s):_____ Dr. _____ DEA No._____ Address _____ Telephone _____	mouth once daily #100 mL
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Myrbetriq Granules	

FDA Prescription Simulation Responses (Aggregate Report)

209 People Received Study
71 People Responded

Study Name: Myrbetriq Granules

Total	21	15	21	14	71
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
LUBRITRICK GRANULES	0	0	1	0	1
MERBETRIC	0	0	1	0	1
MERBETRIC GRANULES	0	0	1	0	1
MERBETRIQ	0	0	1	0	1
MEREBETRIC GRANULES	0	0	1	0	1
MERMETRIC GRANULES	0	0	1	0	1
MERPETRICK GRANULES	0	0	1	0	1
MIRABETRIC GRANULES	0	0	1	0	1
MIRBETRIC GRANULES	0	0	1	0	1
MIRBETRIK	0	0	1	0	1

MIRBETRIK GRANULES	0	0	1	0	1
MIRBETRIQ GRANULES	0	0	1	0	1
MIRPRETIC GRANULES	0	0	1	0	1
MURBETRIC GRANULES	0	0	1	0	1
MYBETRIC	0	0	1	0	1
MYBETRIQ GRANULES	1	0	0	1	2
MYRBETRIC GRANULES	0	0	0	1	1
MYRBETRIQ	0	1	0	0	1
MYRBETRIQ GRANUELS	0	0	0	1	1
MYRBETRIQ GRANULEES	0	0	0	1	1
MYRBETRIQ GRANULES	19	14	6	10	49
MYSBETRIQ GRANULES	1	0	0	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/

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02/05/2021 01:29:48 PM

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02/05/2021 03:17:53 PM