CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208587Orig1s000

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:	24 February 2017
Application Type and Number:	NDA 208587
Product Name and Strength:	Endari (L-glutamine) 5 grams Powder for oral administration
Product Type:	Single-Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Emmaus Medical, Inc.
Panorama #:	2016-11648010
DMEPA Primary Reviewer:	Leeza Rahimi, Pharm.D.
DMEPA Team Leader:	Hina Mehta, Pharm.D.
DMEPA Associate Director (Acting):	Mishale Mistry, Pharm.D., MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Endari***, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by (b) (4) for this product.

1.1 PRODUCT INFORMATION

The following product information is provided in the 30 November 2016 proprietary name submission.

- Intended Pronunciation: en dah' ree
- Active Ingredient: L-glutamine
- Indication of Use: Treatment for sickle cell disease
- Route of Administration: Oral
- Dosage Form: Powder for oral administration
- Strength: 5 grams
- Dose and Frequency: Dosage will be in increments of 5 grams based on weight approximately 0.3 grams/kg per single dose twice daily. Maximum daily dose of 30 grams.
- How Supplied: 5 grams of L-glutamine powder per paper-foil-plastic laminate packet
- Storage: Store in a dry place at room temperature, 25°C, away from direct sunlight
- Container and Closure Systems: The drug will be supplied in packets which contain 5 grams of drug product. The packets will then be housed in a carton that contains divided compartments holding a total of (b) (4) packets or (b) (4) grams of product.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Hematology Products (DHP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 *Components of the Proposed Proprietary Name*

The Applicant indicated in their submission that the proposed name, Endari***, is derived from the word [redacted] (b) (4)

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

2.2.3 *FDA Name Simulation Studies*

Ninety-eight (98) practitioners participated in DMEPA's prescription studies. One participant misinterpreted the name as "Endure". In addition, two participants in the voice study misinterpreted the name as "Enduree" which is a close variation of the marketed antiseptic hand wash products "Endure 100", "Endure 200", "Endure 250", "Endure 300", and "Endure 450". We note that "Endari" contains an extra syllable which provides some phonetic difference between the name pair. Orthographically, the name pair vary in the suffix where Endari*** has a dotted letter 'i' at the 6th position vs. 'e' in Endure. In addition, "Endure" and "Endari" differ both in strength (1%, 0.2%, 62%, 70% vs. 5 mg) and dose (Wash or scrub hands as needed vs. 0.3 g/kg twice daily). We evaluate this name pair in Appendix C.

Sixty-five participants interpreted the name correctly. Appendix B contains the results from the verbal and written prescription studies.

2.2.4 *Comments from Other Review Disciplines at Initial Review*

In response to the OSE, 28 December 2016 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 *Phonetic and Orthographic Computer Analysis (POCA) Search Results*

Table 1 lists the number of names retrieved from our POCA search[b] and also includes names identified from the FDA Prescription Simulation Study and by [redacted] (b) (4)
These names are organized as highly similar, moderately similar or low similarity for further evaluation.

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[a] USAN stem search conducted on 12 December 2016

[b] POCA search conducted on 09 January 2017 in version 4.0.

Table 1. Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	12
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	114
Low similarity name pair: combined match percentage score ≤54%	84

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

Our analysis of the 210 names contained in Table 1 determined 210 names will not pose a risk for confusion as described in Appendices C through H.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Division of Hematology Products (DHP) via e-mail on 21 February 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DHP on 24 February 2017, they stated no additional concerns with the proposed proprietary name, Endari***.

2.2.8 Discussion of Dual Proprietary Name

Emmaus Medical Inc. has proposed two different marketing applications for their L-glutamine, 5 gram oral powder. The first product was approved in 2004 under NDA 021667 with a proprietary name Nutrestore. The product is indicated for treatment of short bowel syndrome in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication. The new proposed name Endari*** submitted under NDA 208587 is indicated for the treatment of sickle cell disease.

Table 2 provides a side-by-side comparison of the two proposed products.

Table 2. Comparison of Endari*** and Nutrestore		
Attribute	**Endari*** **	**Nutrestore**
Application Number	NDA 208587	NDA 021667
Strength	5 grams	5 grams
How Supplied	Oral powder supplied in packets	Oral powder supplied in packets

	which contain 5 grams of drug product. Carton of (b) (4) packets.	which contain 5 grams of drug product. Carton of 84 packets.
Dosing and Administration	The dosage will be in increments of 5 grams based on weight, approximately 0.3 g/kg per single dose. Twice daily. Max dose 30 grams	The recommended dose is 30 grams daily in divided doses (5 g taken 6 times daily. Doses should be taken with meals or snacks at 2-3 hour intervals while awake.
Indication	Treatment of sickle-cell disease	treatment of short bowel syndrome in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication

We have evaluated the risks associated with this naming strategy and do not object to the use of a dual proprietary name in this case.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Frances Fahnbulleh, OSE project manager, at 301-796-0942.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your 30 November 2016 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   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.

3. ***Electronic Drug Registration and Listing System (eDRLS) database***

The electronic Drug Registration and Listing System (eDRLS) was established to supports the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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. 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[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.

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

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.

Three 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 or verbal pronunciation of the drug name. 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 orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

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

	upstroke/downstroke letters present in the names?		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.

<table>
<tr><td></td><td colspan="2">

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 <u>with</u> 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 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?

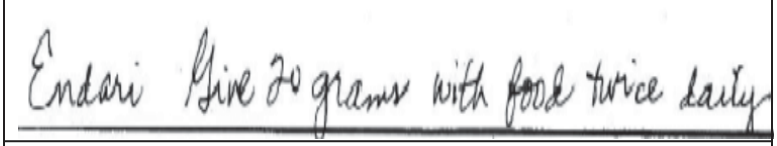
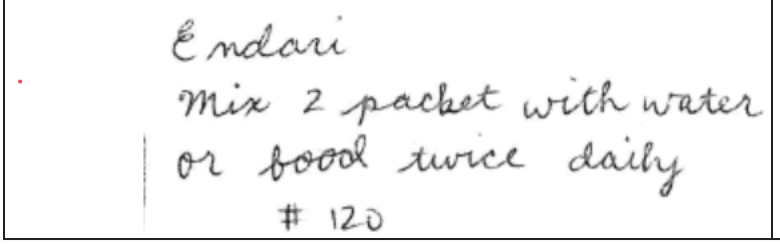
</td></tr>
</table>

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. Endari Study (Conducted on 23 December 2016)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Endari Mix 2 packets with water or food twice daily Dispense #120
Outpatient Prescription: 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Endari

As of Date 1/18/2017

306 People Received Study

98 People Responded

Total	38	31	29	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
EBDARI	0	0	1	1
ENDAREE	0	1	0	1
ENDARI	38	0	27	65
ENDERE	0	1	0	1
ENDERI	0	1	1	2
ENDERY	0	3	0	3
ENDERYEE	0	1	0	1
ENDORI	0	1	0	1
ENDURE	0	1	0	1
ENDUREE	0	2	0	2
ENDUREY	0	1	0	1
ENDURI	0	10	0	10
ENDURIE	0	6	0	6
ENDURY	0	2	0	2
PENDURY	0	1	0	1

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

No.	**Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).**	**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.	Endari***	100	Subject of the study
2.	Endure 100	74	**Phonetic**: Endari*** contains an extra syllable, which provides some phonetic difference between the name pair. Furthermore, the product characteristics of the name pair are different and there is no overlap in dosing which will help minimize the risk for confusion between the products. **Product Characteristics:** **Endure 100 vs. Endari***** Dose: Apply on hands as needed vs. 0.3 g/kg twice daily
3.	Endure 200	74	**Phonetic**: Endari*** contains an extra syllable, which provides some phonetic difference between the name pair. Furthermore, the product characteristics of the name pair are different, and there is no overlap in dosing which will help minimize the risk for confusion between the two products. **Product Characteristics:** **Endure 200 vs. Endari***** **Dose & Frequency**: Wash hands as needed vs. 0.3 g/kg twice daily
4.	Endure 250	74	**Phonetic**: Endari*** contains an extra syllable, which provides some phonetic difference between the name pair. Furthermore, the product characteristics of the name pair are different and there is no overlap in dosing, which will help minimize the risk for confusion between the two products. **Product Characteristic Differences:** **Endure 250 vs. Endari***** **Dose & Frequency**: Apply on hands as needed vs. 0.3 g/kg twice daily

No.	Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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.
5.	Endure 300	74	**Phonetic**: Endari*** contains an extra syllable, which provides some phonetic difference between the name pair. Furthermore, the product characteristics of the name pair are different and there is no overlap in dosing, which will help minimize the risk for confusion between the two products. **Product Characteristic Differences:** **Endure 300 vs. Endari***** **Dose & Frequency**: Apply on hands as needed vs. 0.3 g/kg twice daily
6.	Endure 450	74	**Phonetic**: Endari*** contains an extra syllable, which provides some phonetic difference between the name pair. Furthermore, the product characteristics of the name pair are different and there is no overlap in dosing, which will help minimize the risk for confusion between the two products. **Product Characteristics Differences:** **Endure 450 vs. Endari***** **Dose:** Scrub hands as need prior to surgery vs. 0.3mg/kg twice daily
7.	Endal	73	**Orthographic:** Endal has an upstroke letter 'l' in the fifth position, whereas, Endari*** lacks an upstroke and has a letter 'r' in the fifth position. In addition, Endari*** has a dotted letter 'i' in the 6th position which provides some orthographic difference between the name pair. **Phonetic:** The last syllables of the name pair "dal" in Endal and "ri" in Endari*** sound different. Also, Endari*** has an extra syllable (en dah' ree vs. en dal). **Product Characteristics**: Endal was an OTC combination product which the brand has been discontinued. No generic equivalent is available.

<table>
<tr><th>No.</th><th>Proposed name: Endari***
Established name: L-glutamine
Dosage form: Oral Powder
Strength(s): 5 grams
Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).</th><th>POCA Score (%)</th><th>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.</th></tr>
<tr><td>8.</td><td>Edarbi</td><td>73</td><td>Orthographic: Edarbi has an additional upstroke letter ‘b’ in the 5th position, whereas, Endari*** lacks the upstroke, giving the names different shape. This provides some orthographic difference.
Phonetic: The third syllable of this name pair sound different. The letter string ‘ri’ in Endari*** vs. ‘bi’ in Edarbi have some phonetic differences.

There is no overlap or similarity in strengths and dosing information between the name pair Therefore, there is a minimum risk of confusion between the two products.
Product Characteristic Differences:
Edarbi vs. Endari***
<u>Strengths:</u> 40 mg, 80 mg vs. 5 grams
Edarbi is available in two strengths, therefore its strength would need to be specified.
<u>Dosing:</u> 40 or 80 mg once daily vs. 0.3 grams/kg/dose in increments of 5 grams twice daily with a max dose of 30 grams. The specific dosing for Endari*** is summarized in the table below:
<table>
<tr><th>Weight in kgs.</th><th>Per dose in grams</th><th>Per day in grams</th><th>Packets per dose</th><th>Packets per day</th></tr>
<tr><td>< 30</td><td>5.0</td><td>10.0</td><td>1</td><td>2</td></tr>
<tr><td>30 - 65</td><td>10.0</td><td>20.0</td><td>2</td><td>4</td></tr>
<tr><td>> 65</td><td>15.0</td><td>30.0</td><td>3</td><td>6</td></tr>
</table>
</td></tr>
<tr><td>9.</td><td>Antara</td><td>72</td><td>Orthographic: The name pair starts with different letters 'E' vs. 'A'. The letter ‘i’ vs. ‘a’ in the 6th position also provide some orthographic differences.
Phonetic: The third syllables of the name pair sound different. The last syllable ‘ra’ in Antara phonetically sound different than last syllable ‘ri’ in Endari***.</td></tr>
</table>

No.	Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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.
10.	Dendrid	72	**Orthographic**: Dendrid begins with the letter 'D' which appears orthographically different than the first letter 'E' in Endari***. Additionally, Dendrid has an extra letter 'd' at the 7th position after the letter 'i', which provides further differentiation between the name pair **Phonetic**:. The first syllable in the name Dendrid begins with 'Den' which sounds distinct from the first syllable 'End' in Endari***. Also, Endari*** contains an extra syllable. **Product Characteristic Differences:** **Dendrid vs. Endari***** **Dosing:** 1 drop in each infected eye vs. 0.3 grams/kg/dose
11.	Inderal	70	**Orthographic**: The first letters of the names 'I' vs. 'E' look different when scripted. Inderal has an upstroke letter 'l' in the 6th position whereas, Endari*** has a dotted letter 'i' which may provide some additional orthographic difference. **Phonetic:** The third syllable 'al' in Inderal sounds distinct from the third syllable 'ri' in Endari***. **Product Characteristic Differences:** **Inderal vs. Endari***** **Strength:** 60 mg, 80 mg, 120 mg, 160 mg vs. 5 g
12.	Endaroid (from external study)	77	**Orthographic**: The ending letters, 'oid' in Endarioid vs.'-i' in Endari*** help differentiate the names when scripted. Endaroid has an upstroke letter 'd 'at the end of the name, whereas, Endari*** has no upstroke at the end of the name. **Phonetic**: The third syllable 'roid' in Endaroid sound distinct from the third syllable 'ri' in Endari.***

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.	Encare	66
2.	Endrate	66
3.	Nazarin	62
4.	Endodan	61
5.	Endolor	61
6.	Entre-B	61
7.	Entre-S	61
8.	Empirin	60
9.	Enhancer I	60
10.	Nariz	60
11.	Epidrin	59
12.	Mindal	59
13.	Tindal	59
14.	Embeda	58
15.	Endal Cd	58
16.	Endal-Hd	58
17.	Endep	58
18.	Endocet	58
19.	(b) (4)***	58
20.	Namzaric	58
21.	Banaril	56
22.	Envarsus	55
23.	Cyndal	55
24.	(b) (4)***	55
25.	Denavir	62
26.	Inderide	65
27.	Inderide-40/25	65
28.	Inderide-80/25	65
29.	Inderide La	56
30.	Inderide La 120/50	56
31.	Inderide La 160/50	56
32.	Inderide La 80/50	56
33.	Inderal La	60
34.	Adrenalin	52
35.	Indolar	64
36.	Indinavir	55
37.	Aredia	46
38.	Asendin	52
39.	Benzedrine	52
40.	Danocrine	46
41.	Dexedrine	44
42.	Diar-Aid	51
43.	Dri-Ear	48

No.	Name	POCA Score (%)
44.	Namenda Xr	52
45.	Neo-Dexair	44
46.	Pediarix	52
47.	Renacidin	50
48.	Treanda	51
49.	Duradrin	48
50.	Emadine (external study)	48
51.	Entaprin	68

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: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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.	Enbrel	62	The infixes of the name pair have sufficient orthographic differences. The second syllables of the name pair have sufficient phonetic differences. Also, Endari*** has an extra syllable.
2.	Endur-Acin	62	The letter string '-Acin' in Endur-Acin, and the dash '-' between 'Endur' and 'Acin' provides sufficient orthographic difference with Endari***. The third syllable of this name pair has sufficient phonetic differences. Endur-Acin has an extra syllable and provides sufficient phonetic difference between the name pair.
3.	Entereg	62	The suffixes of the name pair have sufficient orthographic differences. The second and third syllables of the name pair sound different.
4.	Aldara	62	The prefixes of the name pair have sufficient orthographic differences. The first and third syllables of the name pair sound different. **Dosing and route of administration**: Aldara is a topical cream that is applied to a defined treatment area on the face or scalp 2 times per week on defined days of the week (i.e. mondays and thursdays, or Tuesdays and Fridays).

No.	Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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
5.	Edecrin	60	The prefixes and suffixes of the name pair have sufficient orthographic differences. The first, second, and third syllables of the name pair sound different.
6.	Emagrin	60	The infixes and suffixes of the name pair have sufficient orthographic differences. The first, second, and third syllables of the name pair sound different.
7.	Edluar	58	The prefixes and suffixes of the name pair have sufficient orthographic differences. The first, second, and third syllables of the name pair sound different.
8.	Endometrin	56	The letter string '-ometrin' in Endometrin provides sufficient orthographic difference between the name pair. Endometrin has extra syllables which provides sufficient phonetic difference for the name pair.
9.	Enalapril	55	The infixes and suffixes of the name pair have sufficient orthographic differences. The second and third syllables of the name pair sound different. Enalapril has an extra syllable.
10.	Bendeka	55	The prefixes and suffixes of the name pair have sufficient orthographic differences. The first and second syllables of the name pair sound different.
11.	Nardil	58	The first letters of the name pair are different 'N' vs. 'E' when scripted. Endari*** has an upstroke letter 'd' in the third position, whereas Nardil has it in 4th position. The first syllables of the name pair sound different, and Endari*** has an extra syllable.
12.	Android	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. Endari*** has an extra syllable and phonetically sounds different than Android.
13.	Android 10	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. In addition, the modifier in Android will help distinguish the name pair. Endari*** has an extra syllable and the second syllable phonetically sounds different than Android.

No.	Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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
14.	Android 25	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. In addition, the modifier in Android will help distinguish the name pair. Endari*** has an extra syllable and the second syllable phonetically sounds different than Android.
15.	Android 5	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. In addition, the modifier in Android will help distinguish the name pair. Endari*** has an extra syllable and the second syllable phonetically sounds different than Android.
16.	Android-10	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. In addition, the modifier in Android will help distinguish the name pair. Endari*** has an extra syllable and the second syllable phonetically sounds different than Android.
17.	Android-25	65	The letter string '-droid' in Android provides sufficient orthographic differences between the name pair. In addition, the modifier in Android will help distinguish the name pair. Endari*** has an extra syllable and the second syllable phonetically sounds different than Android.
18.	Addaprin	58	The prefixes, infixes, and suffixes of the name pair have sufficient orthographic differences. The first, second, and third syllables of the name pair sound different.
19.	Daranide	48	The prefixes, infixes, and suffixes of the name pair have sufficient orthographic difference. The first, second, and third syllables of the name pair sound different.
20.	Femadrine	50	The prefixes, infixes, and suffixes of the name pair have sufficient orthographic difference. The first, second, and third syllables of the name pair sound different.
21.	Omnaris	64	The prefixes, infixes, and suffixes of the name pair have sufficient orthographic difference. The first, second, and third syllables of the name pair sound different.
22.	Stendra	62	The prefixes, infixes,and suffixes of the name pair have sufficient orthographic difference. The first and second syllables of the name pair sound different. Endari*** contains an extra syllable.
23.	Temodar	60	The prefixes, infixes, and suffixes of the name pair have sufficient orthographic difference. The first, second, and third syllables of the name pair sound different.

No.	Proposed name: Endari*** Established name: L-glutamine Dosage form: Oral Powder Strength(s): 5 grams Usual Dose: 0.3 g/kg per dose twice daily (max dose 30 grams/day).	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
24.	Imdur	57	The prefixes of the name pair have sufficient orthographic differences. The last syllables of the name pair sound different and Endari has an additional syllable.

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

No.	Name	POCA Score (%)
1.	Aldoril	52
2.	Aldoril 15	52
3.	Aldoril 25	52
4.	Ampyra	54
5.	Anoro	48
6.	Ansaid	54
7.	Anspor	49
8.	Antacid I	50
9.	Antepar	54
10.	Anturol	48
11.	Avandaryl	54
12.	Chemdal	52
13.	Edoxaban	37
14.	Elspar	48
15.	Empro	48
16.	Emtriva	52
17.	Emverm	49
18.	Encort	54
19.	Encron	54
20.	Enduronyl	54
21.	Engerix-B	52
22.	Enlon	38
23.	Entyvio	50
24.	Femara	54
25.	Gemzar	54
26.	Indocin	54
27.	Infanrix	52
28.	Inocor	48
29.	Inspra	54
30.	Intal	52

No.	Name	POCA Score (%)
31.	Introl	51
32.	Isonarif	52
33.	Ivderm	52
34.	Moderil	54
35.	Temaril	54
36.	Ventral	52
37.	Ventavis	52

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.	Andryl 200	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
2.	Depinar	58	Brand discontinued with no generic equivalent available. NDA 011208 withdrawn FR effective 04/04/1990.
3.	(b) (4)	66	Proposed proprietary name for NDA 076681 found unacceptable by DMEPA (OSE# 2011-1221). NDA 076681 approved under new proprietary name Kimidess.
4.	Kemadrin	58	Brand discontinued with no generic equivalent available (per RedBook).
5.	Tanderil	66	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
6.	(b) (4) ***	68	Proposed proprietary name for NDA 022279 found unacceptable by DMEPA (OSE# 2010-1691). NDA 022279 approved under new proprietary name Hycofenix.
7.	Phendry	68	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
8.	Enduron	67	Brand discontinued with no generic equivalent available. NDA 012524 withdrawn FR effective 04/18/2014
9.	Encora	66	Brand discontinued with no generic equivalent available.
10.	Epidri	65	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

No.	Name	POCA Score (%)	Failure preventions
11.	End-Zit	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
12.	Tandearil	64	Brand discontinued with no generic equivalent available. NDA 010744 withdrawn FR effective 12/07/2007.
13.	(b) (4) ***	62	Proposed proprietary name for NDA 200490 found unacceptable by DMEPA (OSE# 2010-1758). NDA 200490 approved under (Levonorgestrel and Ethinyl Estradiol Tablets)
14.	(b) (4) ***	62	Proposed proprietary name withdrawn by the Applicant. Product approved under Besponsa
15.	Enkaid	62	Discontinued encainide hydrochloride product with no generic equivalents available.
16.	(b) (4) ***	59	Proposed proprietary name withdrawn by the Applicant. Product approved under new proprietary name, Rogaine.
17.	Encore	58	Veterinary product
18.	Uniparin	58	International product formerly marketed in Australia, Ireland, and United Kingdom.
19.	Estar	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
20.	Eumydrin	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Ardeparin	56	Brand discontinued with no generic equivalent available. NDA 020227 withdrawn FR effective 02/11/2002
22.	Darbid	56	Brand discontinued with no generic equivalent available. NDA 012542 withdrawn FR effective 05/29/2002.
23.	Fansidar	56	Brand discontinued with no generic equivalent available. NDA 018557 withdrawn FR effective 04/18/2012.
24.	(b) (4) ***	56	Alternate proposed proprietary name for ANDA 201887. Primary proposed name, Enskyce found acceptable in OSE Review RCM # 2012-1067. Application approved and marketed under proprietary name, Enskyce.
25.	Syntaris	56	International product marketed in Belgium, Netherlands, the UK, Austria, Czech Republic, Ireland, South Africa, Switzerland, Germany, and Italy.
26.	Daktarin	55	International product marketed in Australia, Belgium, and Mexico.

No.	Name	POCA Score (%)	Failure preventions
27.	Eradacin	52	International product formerly marketed in Ireland and United Kingdom.
28.	Aromadendrin	48	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
29.	Med Aspirin	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
30.	Nadroparin	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
31.	Paredrine	42	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
32.	Predair	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
33.	Renamin	48	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
34.	Renamin 6.5	48	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
35.	Rondamine	46	Product discontinued with no generic available
36.	Tanderil	66	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
37.	Cafedrine	42	Product is not a drug. Ingredient for a multi-ingredient product called Akrinor sold in South Africa.
38.	Denaverine	42	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
39.	Denti Care	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
40.	Denticare	50	International product formerly marketed in Israel.
41.	Depinar	58	Brand discontinued with no generic equivalent available. NDA 011208 withdrawn FR effective 04/04/1990.
42.	(b) (4) ***	50	Proposed proprietary name for IND 077278 found unacceptable by DMEPA (OSE# 2010-1909). NDA 202331 approved under new proprietary name Edarbyclor.

No.	Name	POCA Score (%)	Failure preventions
43.	(b) (4) ***	50	Proposed proprietary name for NDA 202331 found unacceptable by DMEPA (OSE# 2011-703). NDA 202331 approved under new proprietary name Edarbyclor.
44.	Enaprilat	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
45.	Encainide	46	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
46.	A-Phedrin	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
47.	Aleudrin	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
48.	Endafed	64	Brand discontinued with no generic equivalent available

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 (%)
1.	Benicar	59
2.	Lentard	63
3.	Pedi-Dri	62
4.	Sandril	63
5.	(b) (4) ***	55
6.	Android-F	56
7.	Radri	56
8.	Synadrin	56
9.	Ventaire	55
10.	Xenaderm	56
11.	Idenal	57
12.	Indoramin	58
13.	Condrin	60
14.	Zenzedi	59
15.	Advair	60

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

No.	Name	POCA Score (%)
16.	Andec-Tr	58
17.	(b) (4)***	56
18.	(b) (4)***	58
19.	Decara	56
20.	Midrin	56
21.	Pine Tar	58
22.	Zentrip	58
23.	Fentazin	55
24.	Lentaron	58
25.	Amprid	58
26.	Anabar	64
27.	Andro La	56
28.	Andro La 200	56
29.	Innovar	62
30.	Ninlaro	56
31.	Renvela	55
32.	Uni-Dur	59
33.	Invarest	56
34.	Fentora	59
35.	Incurin	57
36.	Indigo	56
37.	Indole	56
38.	Amber	57

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/s/

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