CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

207078Orig1s000

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 6, 2018
Application Type and Number:	NDA 207078
Product Name and Strength:	Lokelma (Sodium Zirconium Cyclosilicate) for oral suspension, 5 grams per packet and 10 grams per packet
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	ZS Pharma
Panorama #:	2017-19223926
DMEPA Safety Evaluator:	Sarah Thomas, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Lokelma, 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 did not submit an external study but referred to the previously submitted external name study, conducted by (b) (4), in the October 4, 2016 proprietary name submission from the last review cycle.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Lokelma, under IND 108951 on March 19, 2014. Lokelma was found conditionally acceptable under IND 108951 on July 3, 2014.[a] Subsequently, the Applicant submitted the proposed name, Lokelma, for review on June 1, 2015 under NDA 207078. Lokelma was again found conditionally acceptable under NDA 207078 on August 11, 2015.[b] NDA 207078 received a Complete Response on May 26, 2016.

The Applicant resubmitted the name, Lokelma, for review as a part of their Class 2 resubmission on October 4, 2016 under NDA 207078. Lokelma was found conditionally acceptable under NDA 207078 on December 20, 2016.[c] NDA 207078 received a Complete Response on March 16, 2017.

The Applicant submitted the name, Lokelma, for review as a part of their Class 2 resubmission on November 22, 2017 under NDA 207078. In this Class 2 resubmission, we note that the dosing information changed, as follows:

	October 4, 2016 submission	November 22, 2017 submission
Initial starting dose for maintenance treatment	(b) (4) 10 g orally once daily	(b) (4) orally once daily
Maximum dose	(b) (4) orally once daily	15 g orally once daily

1.2 PRODUCT INFORMATION

[a] Stewart, J. Proprietary Name Review for Lokelma (IND 108951). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 JULY 3. Panorama No.: 2014-17132.

[b] Gao, T. Proprietary Name Review for Lokelma (NDA 207078). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 AUG 11. Panorama No.: 2015-600670.

[c] Thomas, S. Proprietary Name Review for Lokelma (NDA 207078). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 DEC 20. Panorama No.: 2016-10575174.

The following product information is provided in the November 22, 2017 proprietary name submission and the December 5, 2017 amendment.

- Intended Pronunciation: lo-KELL-ma
- Active Ingredient: sodium zirconium cyclosilicate
- Indication of Use: Treatment of hyperkalemia
- Route of Administration: Oral
- Dosage Form: For oral suspension
- Strength: 5 grams per packet, and 10 grams per packet
- Dose and Frequency:
    - For initial treatment of hyperkalemia, the recommended dose is 10 g administered 3 times a day for up to 48 hours.
    - For maintenance treatment, the recommended initial maintenance dosage is (b) (4) once daily. Monitor serum potassium and adjust the dose in 5 g increments between 5 g every other day and 15 g daily, based on serum potassium level and desired target range.
- How Supplied: white powder in foil-lined packets, contained in boxes of 30 count 5 grams and 30 count 10 gram packets
- Storage: Store LOKELMA at 15°C-30°C (59°F-86°F).

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. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Cardiovascular and Renal Products (DCRP) 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[d].

[d] USAN stem search conducted on December 1, 2017.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Lokelma, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error. We previously evaluated the letters "Lo-K" (lowering potassium) in "Lokelma", and did not find this misleading or that it misrepresents the proposed product in our previous review.[c] We maintain our previous position.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, December 8, 2017 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety-six practitioners participated in DMEPA's prescription studies. Of note, when evaluating the response "Lakelma" (n=1 response in inpatient prescription study), we identified the close hits "Velma" and "Lobelia". Velma and Lobelia are further evaluated in Appendix E. Also, one participant responded, "looks like sounds like Lotemax." We evaluated Lotemax in Appendices D and E in two prior reviews[e,f] and we maintain our position that the name pair has sufficient orthographic and phonetic differences. The other responses did not overlap with any currently marketed products nor did the other responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[g] identified 31 names with the combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score of ≥70%**.** We had identified and evaluated 106 names in our previous proprietary name reviews.[a,b,c] We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience as well as the change in dosing information (See Section 1.1), which may have altered our previous conclusion regarding the acceptability of the name. We agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 3 names not previously analyzed. These names are included in Table 1 below.

---

[e] Stewart, J. Proprietary Name Review for Lokelma (IND 108951). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 JULY 3. Panorama No.: 2014-17132.

[f] Gao, T. Proprietary Name Review for Lokelma (NDA 207078). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 AUG 11. Panorama No.: 2015-600670.

[g] POCA search conducted on November 8, 2016 in version 4.2. POCA tool updated to incorporate a revised orthographic algorithm.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

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

Table 1. Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	4
Low similarity name pair: combined match percentage score ≤54%	1

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

Our analysis of the 5 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on January 29, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on February 5, 2018, they stated no additional concerns with the proposed proprietary name, Lokelma.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Darrell Lyons, OSE project manager, at 301-796-4092.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your November 22, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

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. [h]

[h] 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[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 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.,

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

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 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

<table>
<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. Lokelma Study (Conducted on December 13, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: DATE TIME Lokelma 10g po three times a day x 48hrs Outpatient Prescription: Patient _____ Date 12/8/17 Address _____ ℞ Lokelma (b) (4) Take 1 po daily as directed #30 MEDWATCH 1-800-FDA-1088 Refill(s):_____ Dr. Ose DEA No._____ Address _____ Telephone _____	Lokelma (b) (4) Take one by mouth daily as directed Dispense #30

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Lokelma

As of Date 12/27/2017

294 People Received Study
96 People Responded

Study Name: Lokelma

Total	36	27	33	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
FOKELMA	1	0	0	1
JOKELMA	1	0	0	1
LABELMA	0	0	2	2
LABELMO	0	0	1	1
LAKELMA	0	0	1	1
LOBELMA	0	0	10	10
LOBELMO	0	0	9	9
LOCALMA	0	10	0	10
LO-CALMA	0	1	0	1
LOCAMEL	0	1	0	1
LOKALMA	0	2	0	2
LOKELMA	0	10	5	15
LOKELMO	0	0	2	2
LOKELVA	0	1	0	1
LOPELMA	0	0	2	2
LOPELMO	0	0	1	1
LOW-CALMA	0	1	0	1
TOKELIMA	1	0	0	1
TOKELMA	32	0	0	32
TOKILMA	1	0	0	1
ZOCAIVA	0	1	0	1

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

No.	**Proposed name:** Lokelma **Established name:** Sodium Zirconium Cyclosilicate **Dosage form:** for oral suspension **Strength(s):** 5 g or 10 g powder per packet **Usual Dose:** For initial treatment of hyperkalemia, 10 g by mouth three times daily for 48 hours; For maintenance treatment, starting dose of (b)(4) once daily with dose titrated in 5 g increments between maximum dose of 15 g once daily and a minimum dose of 5 g every other day based on desired target potassium range	POCA Score (%)	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
	N/A		

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
	N/A	

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Lokelma **Established name:** Sodium Zirconium Cyclosilicate **Dosage form:** for oral suspension **Strength(s):** 5 g or 10 g powder per packet **Usual Dose:** For initial treatment of hyperkalemia, 10 g by mouth three times daily for 48 hours; For maintenance treatment, starting dose of (b) (4) once daily with dose titrated in 5 g increments between maximum dose of 15 g once daily and a minimum dose of 5 g every other day based on desired target potassium range	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.	Kemagel	45	This name pair has sufficient orthographic and phonetic differences. Kemagel is a part of the product name, "Kemagel Pain Relief" gel.
2.	Lobelia	64	Lobelia is a homeopathic product. This name pair has sufficient orthographic and phonetic differences.
3.	Lonhala	56	This name pair has sufficient orthographic and phonetic differences.
4.	Velma	60	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
	N/A	

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

No.	Name	POCA Score (%)	Failure preventions
	N/A		

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

No.	Name	POCA Score (%)
5.	(b) (4) ***	58

Appendix I: Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name
	N/A

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SARAH E THOMAS
02/06/2018

CHI-MING TU
02/06/2018

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:	December 20, 2016
Application Type and Number:	NDA 207078
Product Name and Strength:	Lokelma (Sodium Zirconium Cyclosilicate) powder for suspension, 5 grams and 10 grams
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	ZS Pharma, Inc.
Panorama #:	2016-10575174
DMEPA Primary Reviewer:	Sarah Thomas, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Lokelma, 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 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Lokelma, under IND 108951 on March 19, 2014. Lokelma was found conditionally acceptable under IND on July 3, 2014.[a] Subsequently, the Applicant submitted the name, Lokelma, for review on June 1, 2015 under NDA 207078. Lokelma was again found conditionally acceptable under NDA on August 11, 2015.[b]

The Applicant resubmitted the name, Lokelma, for review as a part of their Class 2 resubmission on October 4, 2016 under NDA 207078. In the Class 2 resubmission, we noted the maximum dose for maintenance therapy changed (i.e. changed from 15 g by mouth once daily to (b) (4) g by mouth once daily).

1.2 PRODUCT INFORMATION

The following product information is provided in the October 4, 2016 proprietary name submission.

- Intended Pronunciation: lo-KELL-ma
- Active Ingredient: Sodium Zirconium Cyclosilicate
- Indication of Use: (b) (4) indicated for the treatment of hyperkalemia (b) (4)
- Route of Administration: Oral
- Dosage Form: Powder for oral suspension
- Strength: 5 g per packet; 10 g for packet
- Dose and Frequency:
    - For initial treatment of hyperkalemia, 10 g by mouth three times daily for 48 hours
    - For maintenance treatment, starting dose of (b) (4) 10 g once daily with dose titrated in 5 g increments between maximum dose of (b) (4) g once daily and a minimum dose of 5 g every other day based on desired target potassium range

---

[a] Stewart, J. Proprietary Name Review for Lokelma (IND 108951). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 JULY 3. Panorama No.: 2014-17132.

[b] Gao, T. Proprietary Name Review for Lokelma (NDA 207078). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 AUG 11. Panorama No.: 2015-600670.

- How Supplied: foil-lined packets in boxes of 30-count 5 g packets and 30-count 10 g packets
- Storage: Store at 15°C-30°C (59°F-86°F).
- Container and Closure Systems: Foil-lined packet

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 Cardiovascular and Renal Products (DCRP) 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[c].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Lokelma, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error. Of note, "Lokelma" contains the letters "Lo-k", which may be interpreted as referring to the product's indication of lowering potassium in patients with hyperkalemia. We do not find this misleading or that is misrepresents the proposed product.

2.2.3 FDA Name Simulation Studies

Ninety-five practitioners participated in DMEPA's prescription studies. Thirty participants interpreted Lokelma correctly in the inpatient and outpatient handwritten prescription studies and in the verbal prescription study. Common misinterpretations of the prefix "Lo-" in "Lokelma" include misinterpreting "Lo-" as "Le-" (n=5 in the inpatient prescription study). Common misinterpretations of the infix "-kel-" in "Lokelma" include misinterpreting "-kel-" as "-cal-" (n=15 in the verbal prescription study) and "-kal-" (n=5 in the verbal prescription study). Common misinterpretations of the suffix "-ma" in "Lokelma" include misinterpreting "-ma" as "-ina" (n=2 in the inpatient prescription study, n=17 in the outpatient prescription study) and "-ima" (n=3 in the inpatient prescription study, and n=5 in the outpatient prescription study).

In addition, one practitioner reported "strength looks like 59 m" for the outpatient prescription study. We searched eDRLS for names of concern for products with the strength 59, and

[c] USAN stem search conducted on November 7, 2016.

retrieved 3 results. The 3 resulting names do not look or sound like the proposed name, "Lokelma," and all 3 names have a combined POCA score of ≤20. Thus, no additional names of concern were identified from eDRLS.

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

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 20, 2016 e-mail, the Division of Cardiovascular and Renal Products (DCRP) 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

Our POCA search identified 28 names with the combined score of ≥55%. We had identified and evaluated 92 names in our previous proprietary name reviews.[a,b] After comparing the names, 14 of the 28 names were previously included in our evaluation as a part of the 92 names from our previous review. Thus, only 14 names were newly identified.

We reevaluated these 92 names considering lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that the maximum maintenance therapy dose recommendation for Lokelma has changed since our previous proprietary name review (e.g., (b) (4) from 15 g by mouth once daily to (b) (4) g by mouth once daily). With this change in mind, we reevaluated and agreed with the findings from our previous reviews for the names evaluated previously.

Table 1 lists the 14 newly identified names with the combined orthographic and phonetic score of ≥55% retrieved from our POCA search[d]. These names are organized as highly similar, moderately similar or low similarity for further evaluation. Of note, the additional names from the submitted (b) (4) external name study have already been evaluated in our previous review and so are not included again in Table 1.

Table 1. POCA Search Results	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	12
Low similarity name pair: combined match percentage score ≤54%	2

[d] POCA search conducted on November 8, 2016 in version 4.0. POCA tool updated to incorporate a revised orthographic algorithm.

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

Our analysis of the 14 names contained in Table 1 determined 14 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 Cardiovascular and Renal Products (DCRP) via e-mail on December 9, 2016. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on December 19, 2016, they stated no additional concerns with the proposed proprietary name, Lokelma.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Darrell Lyons, OSE project manager, at 301-796-4092.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your October 4, 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. [e]

[e] 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 medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
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 50% 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 with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it 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, etc.) may be limited when the strength or dose overlaps. We review 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 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%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA 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. Lokelma Study (Conducted on 10/25/2016)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: DATE / TIME: Lokelma 10mg PO TID x 48 hrs Outpatient Prescription: Patient _____ Date _____ Address _____ Rx Lokelma (b) (4) qm 1 PO QD as directed #30 MEDWATCH 1-800-FDA-1088 Refill(s):_____ Dr. _____ DEA No._____ Address _____ Telephone _____	Lokelma (b) (4) Take 1 po daily as directed Dispense 30

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Lokelma

As of Date 11/10/2016

			315 People Received Study 95 People Responded	
Study Name: Lokelma				
Total	**31**	**33**	**31**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
LEKELINA	0	0	1	1
LEKELMA	0	0	4	4
LOCALMA	0	15	0	15
LOKALMA	0	5	0	5
LOKEANA	1	0	0	1
LOKEHNA	1	0	0	1
LOKELIMA	5	0	3	8
LOKELINA	16	0	0	16
LOKELIVA	0	0	2	2
LOKELMA	7	4	19	30
LOKLMA	0	0	1	1
LOKOELINA	1	0	0	1
LOPALMA	0	2	0	2
LOPELMA	0	1	0	1
LORPARMA	0	1	0	1
LOTALMA	0	1	0	1
LOTALVA	0	1	0	1
LOTELMA	0	1	0	1
LOTELPA	0	1	0	1
LOVELINA	0	0	1	1
LYMPHTHALMA	0	1	0	1

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

No.	**Proposed name:** Lokelma **Established name:** Sodium Zirconium Cyclosilicate **Dosage form:** Powder for suspension **Strength(s):** 5 g or 10 g **Usual Dose:** For initial treatment of hyperkalemia, 10 g by mouth three times daily for 48 hours; For maintenance treatment, starting dose of (b) (4) 10 g once daily with dose titrated in 5 g increments between maximum dose of (b) (4) g once daily and a minimum dose of 5 g every other day based on desired target potassium range	**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.	N/A		

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	N/A	

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Lokelma **Established name:** Sodium Zirconium Cyclosilicate **Dosage form:** Powder for suspension **Strength(s):** 5 g or 10 g **Usual Dose:** For initial treatment of hyperkalemia, 10 g by mouth three times daily for 48 hours. For maintenance treatment, starting dose of (b) (4) 10 g once daily with dose titrated in 5 g increments between maximum dose of (b) (4) g once daily and a minimum dose of 5 g every other day based on desired target potassium range.	**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.	Evomela	54; Orthographic 71	The prefixes, infixes, and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Evomela contains one extra syllable.
2.	(b) (4) ***	68; Phonetic 76	The suffixes of this name pair have sufficient orthographic differences. The third syllables of this name pair sound different. The proposed Lokelma is available in multiple, non-overlapping strengths (5 g and 10 g), which differ from the strengths of the proposed (b) (4) *** (b) (4) A strength must be specified for the dispensing of Lokelma and (b) (4) ***, thus providing differentiating product characteristics.
3.	Pleo Alkala	55; Orthographic 74	When considering the modifier "Alkala," the prefixes, infixes, and suffixes of this name pair have sufficient orthographic differences, and the first, second, and third syllables sound different. Pleo Alkala also contains 2 extra syllables. Without consideration of the modifier, the prefixes, infixes, and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Lokelma contains one extra syllable.

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

No.	Name	POCA Score (%)
1.	N/A	

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

No.	Name	POCA Score (%)	Failure preventions
1.	Leucomax	57	International product marketed in Germany, Canada, Mexico, United Kingdom, and other countries.
2.	Lo Femenal	54; Orthographic 72	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
3.	Lorelco	55	Brand discontinued with no generic equivalents available per Micromedex Redbook and Drugs@FDA.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Alkeran	56
2.	Alocane	58
3.	(b) (4)***	59
4.	Blockade	58
5.	Calmol	56
6.	Calmol 4	56
7.	Evacalm	58
8.	(b) (4)***	59

Appendix I: Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name
1.	N/A

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SARAH E THOMAS
12/20/2016

CHI-MING TU
12/21/2016

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:	August 11, 2015
Application Type and Number:	NDA 207078
Product Name and Strength:	Lokelma (sodium zirconium cyclosilicate) powder for suspension, 5 grams and 10 grams
Product Type:	Singe ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	ZS Pharma, Inc.
Panorama #:	2015- 600670
DMEPA Primary Reviewer:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Lokelma, 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 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Lokelma, under IND 108951 on March 29, 2014. Lokelma was found conditionally acceptable under IND on July 18, 2014.

Subsequently, the Applicant submitted the name, Lokelma, for review on June 1, 2015 under NDA 207078.

1.2 PRODUCT INFORMATION

The following product information is provided in the June 1, 2015 proprietary name submission.

- Intended Pronunciation: lo-KELL-ma
- Active Ingredient: sodium zirconium cyclosilicate
- Indication of Use: Treatment of hyperkalemia (b) (4)
- Route of Administration: oral
- Dosage Form: powder for oral suspension
- Strength: 5 g per package, 10 g per package
- Dose and Frequency:
  - (b) (4)
- How Supplied: 1 box of 30 count 5g packets, 1 box of 30 count 10g packets
- Storage: (b) (4)
- Container and Closure Systems: a foil-lined packet
- Reference Listed Drug: not applicable

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 Cardiovascular and Renal Products (DCRP) 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[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Lokelma in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Seventy-three practitioners participated in DMEPA's prescription studies. Fifty-six practitioners interpreted the name correctly as Lokelma. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, June 10, 2015 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from the external name study, conducted by (b) (4).

[1]USAN stem search conducted on June 29, 2015.

[2] POCA search conducted on June 24, 2015.

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	33
Low similarity name pair: combined match percentage score ≤49%	7

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

Our analysis of the 41 names contained in Table 1 determined 41 names will not pose a risk for confusion as described in Appendices C through H.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on July 9, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on July 13, 2015, they stated no additional concerns with the proposed proprietary name, Lokelma.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Darrell Lyons, OSE project manager, at 301-796-4092.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your June 1, 2015 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.

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. [3]

[3] 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 medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
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 50% 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 ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

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 with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it 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, etc.) may be limited when the strength or dose overlaps. We review 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 do 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 ≥50% 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: o 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. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o 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 ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA 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. Lokelma Study (Conducted on June 12, 2015)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Lokelma 10g po TIDX (b) (4) hrs	Lokelma (b) (4) orally once daily Dispense #1 box
Outpatient Prescription: Lokelma (b) (4) po once daily #1 Box	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Lokelma

As of Date 7/7/2015

245 People Received Study

73 People Responded

Total	22	21	30	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
COKELMA	1	0	0	1
LOCALMA	0	3	0	3
LOCELMA	0	2	0	2
LOCHELMA	0	1	0	1
LOKALMA	0	1	0	1
LOKEKMA	1	0	0	1
LOKELA	0	1	0	1
LOKELMA	19	9	28	56
LO-KELMA	0	1	0	1
LOKELMA 10 MG	0	0	1	1
LOKELME	1	0	0	1
LOKELVA	0	1	0	1
LOKELVY	0	1	0	1
LOQUELMA	0	1	0	1
LOTELMA	0	0	1	1

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

No.	**Proposed name:** Lokelma **Established name:** sodium zirconium cyclosilicate **Dosage form:** Powder for suspension **Strength(s):** 5 grams, 10 grams **Usual Dose:** 5 grams every other day to 15 grams once daily	**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.	LOKELMA	100	Name is the subject of the review

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	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.	LAPELGA***	69	
2.	LAXMAR	54	
3.	LESSINA	51	
4.	LESSINA-21	51	
5.	LESSINA-28	51	
6.	LIALDA	57	

No.	Name	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
7.	(b) (4)***	65	The infixes between the name pair have sufficient orthographic differences. The second syllables of the name pair sound different. Additionally, (b) (4) compared to Lokelma. Lokelma has two strengths (5 grams and 10 grams) whereas (b) (4) . Additionally, the proposed Lokelma doses (5g or 10g) and the proposed (b) (4) do not overlap.
8.	LORYNA	50	
9.	(b) (4)***	52	
10.	(b) (4)***	50	
11.	LUNESTA	51	
12.	LUTERA	55	
13.	(b) (4)***	50	

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Lokelma **Established name:** sodium zirconium cyclosilicate **Dosage form:** Powder for suspension **Strength(s):** 5 grams, 10 grams **Usual Dose:** 5 grams every other day to 15 grams once daily	**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.	Lenvima	52	The infix of this name pair has sufficient orthographic differences. The first and second syllables of this name pair sound different.
2.	Leukeran	58	The suffix of this name pair has sufficient orthographic differences. The third syllables of this name pair sound different.
3.	Lokara	64	The suffix of this name pair has sufficient orthographic differences. The third syllables of this name pair sound different.
4.	Lok-pak	53	The suffix of this name pair has sufficient orthographic differences. The second syllables of this name pair sound different. Lokelma contains an extra syllable.
5.	Lok-pak-n	52	The suffix of this name pair has sufficient orthographic differences. The second and third syllables of this name pair sound different.
6.	Loqua	50	The infix and suffix of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different. Lokelma contains an extra syllable.
7.	Lotemax	57	The suffix of this name pair has sufficient orthographic differences. The second and third syllables of this name pair sound different.

No.	**Proposed name:** Lokelma **Established name:** sodium zirconium cyclosilicate **Dosage form:** Powder for suspension **Strength(s):** 5 grams, 10 grams **Usual Dose:** 5 grams every other day to 15 grams once daily	**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**
8.	Lotrel	56	The suffix of this name pair has sufficient orthographic differences. The second syllables of this name pair sound different. Lokelma contains an extra syllable.
9.	(b) (4)***	53 (O70)	The infix and suffix of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different. Lokelma contains an extra syllable.
10.	Low-quel	54	The infix and suffix of this name pair have sufficient orthographic differences. The second syllables of this name pair sound different. Lokelma contains an extra syllable.
11.	Lunelle	50	The infix and suffix of this name pair have sufficient orthographic differences. The second and third syllables of this name pair sound different.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Colesevelam	36
2.	Lamisil	36
3.	Levemir	40
4.	Lithium	36
5.	Lopressor	34
6.	Lotensin	43
7.	Lovaza	48

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.	DARCALMA	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
2.	LASMA	54	International product marketed in Indonesia.
3.	LOBELINE	52	Name identified in RxNorm database. Product is an alkaloid found in "Indian tobacco" and has been used as a smoking cessation aid. However, we were unable to find product characteristics in commonly used drug databases.
4.	LORELCO	52	Discontinued product with no generic equivalent available.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	CALOMEL	50
2.	CLODERM	56
3.	CLOFERA	52
4.	CLOMICALM	52
5.	GLO-SEL	50

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

TINGTING N GAO
08/11/2015

CHI-MING TU
08/11/2015