CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210660Orig1s000

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:	March 11, 2019
Application Type and Number:	NDA 210660
Product Name and Strength:	Elcys (cysteine hydrochloride)[a] injection 50 mg/mL
Total Product Strength:	500 mg/10 mL[b]
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Exela Pharma Sciences, LLC (Exela)
Panorama #:	2018- 28050621
DMEPA Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA Team Leader:	Sarah K. Vee, Pharm.D.

[a]Established name of this product changed from [redacted] (b) (4) to "cysteine hydrochloride", as determined by Office of Pharmaceutical Quality (OPQ) during the review cycle.

[b]Presentation of strength statement is under review with OPQ and DGIEP.

APPEARS THIS WAY ON ORIGINAL

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Elcys, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Exela did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Exela previously submitted the proposed proprietary name, (b) (4) on July 14, 2017 under NDA 210660. We found the name (b) (4) acceptable on October 10, 2017[c]. However, Exela withdrew (b) (4) on December 22, 2018, due to an objection from the United States Patent & Trademark Office for (b) (4) on the basis that (b) (4) an over the counter (OTC) pain medication, was previously registered to another company. Thus, Exela submitted Elcys for review on December 14, 2018.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on December 14, 2018.

- Intended Pronunciation: el cee s
- Active Ingredient: cysteine hydrochloride
- Indication of Use: Elcys is indicated to meet the nutritional requirements of newborn infants requiring total parenteral nutrition (TPN); and of adult and pediatric patients with severe liver disease who may have impaired enzymatic processes and require TPN. It can also be added to amino acid solutions to provide a more complete profile of amino acids for protein synthesis.
- Route of Administration: intravenous
- Dosage Form: injection
- Strength: 500 mg/10 mL (50 mg/mL)[b]
- Dose and Frequency: The recommended dosage of Elcys from birth through adults is shown in Table 1.

[c]Barlow, M. Proprietary Name Review for (b) (4) (NDA 210660). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Oct 10. Panorama No. 2017-16394840.

Age	Recommended Protein[a] Requirement (g/kg/day)[1]	Recommended Elcys Dosage (mg cysteine/g AA)	Recommended Elcys Dosage (mg cysteine/kg/day)
Preterm and term infants less than 1 month of age	3 to 4	15	45 to 60
Pediatric patients 1 month to less than 1 year of age	2 to 3	15	30 to 45
Pediatric patients 1 year to 11 years of age	1 to 2	15	15 to 30
Pediatric patients 12 years to 17 years of age	0.8 to 1.5	5	4 to 7.5
Adults: Stable Patients	0.8 to 1	5	4 to 5
Adults: Critically Ill Patients[b]	1.5 to 2	5	7.5 to 10

AA = Amino Acid

[a] Protein is provided as amino acids. When infused intravenously, amino acids are metabolized and utilized as the building blocks of protein.

[b] Includes patients requiring more than 2 to 3 days in the intensive care unit with organ failure, sepsis or postoperative major surgery. Do not use in patients with conditions that are contraindicated *[see Contraindications (4)]*

- How Supplied: 500 mg/10 mL (50 mg/mL) in 10 mL single-dose vials, packaged as 10 per carton
- Storage: Store at 20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature]. Avoid excessive heat. Protect from freezing.
- Reference Listed Drug/Reference Product: Cysteine Hydrochloride Injection, USP, 7.25% (NDA 19523)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Elcys would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Gastroenterology and Inborn Errors Products (DGIEP) concurred with the findings of OPDP's assessment for Elcys.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Exela indicated in their submission that the proposed proprietary name, Elcys, is derived from the basic term L-cysteine, the active ingredient of the drug product. The prefix ('El') is the phonetic for "L" and the suffix ('cys') is from the word "Cysteine". 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 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 10, 2019 e-mail, the Division of Gastroenterology and Inborn Errors Products (DGIEP) did not forward any comments or concerns relating to Elcys at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred and four (n=104) practitioners participated in DMEPA's prescription studies for Elcys. Two voice study participants interpreted the proposed proprietary name Elcys as 'Alcys' or 'Alsis' which are close variations to the over-the-counter product Alcis. Another voice study participant interpreted Elcys as 'Alsess' which is a close variation to the marketed product, Alesse. Two outpatient participants interpreted Elcys as 'Elaquis' and 'Elquis', which are close variations to the marketed product, Eliquis. Appendix B contains the results from the verbal and written prescription studies.

Despite these close hits in the name simulation study, we find that these name pairs have minimal potential for confusion due to the following:

Elcys vs. Alcis
Both names start with different letters (E vs. A). Additionally, Elcys contains a downstroke letter 'y' in the 4th position, which is absent in Alcis, which provides some orthographic differences. Alcis is an over-the-counter topical cream which is massaged onto the muscles, joints or affected area up to three to four times daily. A prescription/order for Alcis would likely be written as 'Apply to affected area' or 'use as directed'. The dose of Elcys is weight-based, depending on patient age and stability. Therefore, there is no overlap in dose or frequency. Furthermore, Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this

[d] USAN stem search conducted on January 7, 2019.

scenario, due to the above-mentioned factors, we find this name pair acceptable. See Appendix C for the evaluation of this name pair.

Elcys vs. Alesse
The names start with different letters (E vs. A). Elcys has a downstroke letter 'y' in its suffix which is absent in Alesse, providing some orthographic differences. The second syllable ('cys' vs. 'esse') provide some phonetic differences. The dose of Alesse is 1 tablet by mouth once daily or 'use as directed'. The dose of Elcys is weight-based, depending on patient age and stability. Therefore, there is no overlap in dose. Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable. See Appendix E for the evaluation of this name pair.

Elcys vs. Eliquis
The length of the names differs by two letters, which provides some orthographic differences. Eliquis has an additional syllable. The second/third syllable ('cys' vs. 'quis') provide sufficient phonetic differences. Eliquis is available in 2.5 mg and 5 mg tablets. The strength/dose of Eliquis will be specified on a prescription/medication order. Elcys is available in a single strength (500 mg/10 mL [50 mg/mL]), which does not overlap with that of Eliquis. Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable. See Appendix E for the evaluation of this name pair.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results
Our POCA search[e] identified 25 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity
Table 1 lists the number of names retrieved from our POCA search and FDA simulation study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

[e] POCA search conducted on January 7, 2019 in version 4.3

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	2
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	23
Low similarity name pair: combined match percentage score ≤54%	2

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

Our analysis of the 27 names contained in Table 1 determined none of the names will pose a risk for confusion with Elcys 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 Gastroenterology and Inborn Errors Products (DGIEP) via e-mail on March 8, 2019. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Gastroenterology and Inborn Errors Products (DGIEP) on March 11, 2019, they stated no additional concerns with the proposed proprietary name, Elcys.

3 CONCLUSION

The proposed proprietary name, Elcys, is acceptable.

If you have further questions or need clarifications, please contact Shawnetta Jackson, OSE project manager, at 301-796-4952.

3.1 COMMENTS TO EXELA PHARMA SCIENCES, LLC

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

If any of the proposed product characteristics as stated in your submission, received on December 14, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

2. *Phonetic and Orthographic Computer Analysis (POCA)*

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. Misbranding Assessment: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. Safety Assessment: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. 6F[f]

[f] 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[7F[g]]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength

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

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
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 <u>with</u> overlapping or similar strengths or doses.

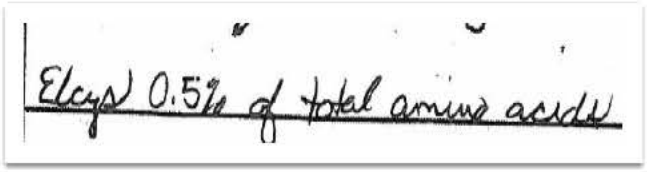
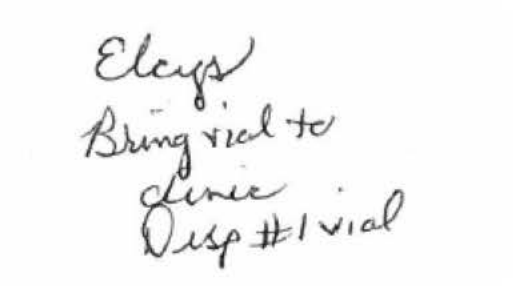
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

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

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: **Prescription Simulation Samples and Results**

Figure 1. Elcys Study (Conducted on December 18, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Elcys Bring vial to clinic Disp #1 vial
Outpatient Prescription:  	

FDA Prescription Simulation Responses (Aggregate Report)

307 People Received Study
104 People Responded

Study Name: Elcys

Total	62	19	23	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
ALCYS	0	1	0	1
ALSESS	0	1	0	1
ALSIS	0	1	0	1
ECLYS	1	0	0	1
ELAQUIS	1	0	0	1
ELAYS	3	0	1	4
ELCRY	0	0	1	1

ELCYS	50	0	18	68
ELCYS 0.5%	0	0	1	1
ELEYS	5	0	2	7
ELOYS	1	0	0	1
ELQUIS	1	0	0	1
ELSIF	0	3	0	3
ELSIS	0	4	0	4
ELSYPHY	0	1	0	1
ELSYS	0	2	0	2
HALSIS	0	1	0	1
HASIS	0	1	0	1
HELSIF	0	1	0	1
HELSIFS	0	1	0	1
HELSIS	0	1	0	1
HELSYS	0	1	0	1

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

No.	Proposed name: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[h]	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.	Elcys	100	This name is the subject of this review.
2.	(b) (4)	92	Previous proposed proprietary name for this NDA; name withdrawn by the Applicant on 12/22/2018.
3.	Alcis	78	Both names start with different letters (E vs. A). Additionally, Elcys contains a downstroke letter 'y' in the 4th position, which is absent in Alcis, which provides some orthographic differences. In addition to the above orthographic differences, the following differences in product characteristics may also help to mitigate the risk of errors: Dose/Frequency: Alcis is an over-the-counter topical cream which is massaged onto the muscles, joints or affected area up to three to four times daily. A prescription/order for Alcis would likely be written as 'Apply to affected area' or 'use as directed'. The dose of Elcys is weight-based, depending on patient age and stability. There is no overlap in dose/frequency between the products.

[h] *Preterm and term infants less than 1 month of age:* 45 to 60 mg cysteine/kg/day; *Pediatric patients 1 month to less than 1 year of age:* 30 to 45 mg cysteine/kg/day; *Pediatric patients 1 year to 11 years of age:* 15 to 30 mg cysteine/kg/day; *Pediatric patients 12 years to 17 years of age:* 4 to 7.5 mg cysteine/kg/day; *Adult stable patients:* 4 to 5 mg cysteine/kg/day; *Adults critically ill patients:* 7.5 to 10 mg cysteine/kg/day

No.	Proposed name: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[h]	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.
			Setting of Use: Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable.

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-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: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[i]	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
4.	Eliphos	60	This name pair has sufficient orthographic and phonetic differences.
5.	Emcyt	60	Elcys contains an upstroke letter 'l' in the 2nd position, which is absent in Emcyt. Emcyt has an upstroke letter 't' in the last position of the name, which is absent in Elcys. These differences provide sufficient orthographic differences. The ending sound of the first syllable ('El vs. 'Em') and the ending sounds of the second syllable ('cys' vs. 'cyt') provide some phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: Dose/frequency: The dose of Emcyt is 14 mg/kg or one 140 mg capsule for each 10 kg of body weight, divided into 3 to 4 doses. A prescription/order for Emcyt would likely be "XX capsules by mouth three to four times daily". The dose of Elcys is weight-based, depending on patient age and stability. Setting of Use: Elcys will be used as an additive in TPN solutions, which in

[i] *Preterm and term infants less than 1 month of age:* 45 to 60 mg cysteine/kg/day; *Pediatric patients 1 month to less than 1 year of age:* 30 to 45 mg cysteine/kg/day; *Pediatric patients 1 year to 11 years of age:* 15 to 30 mg cysteine/kg/day; *Pediatric patients 12 years to 17 years of age:* 4 to 7.5 mg cysteine/kg/day; *Adult stable patients:* 4 to 5 mg cysteine/kg/day; *Adults critically ill patients:* 7.5 to 10 mg cysteine/kg/day

No.	Proposed name: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[i]	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
			clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable.
6.	Elelyso	58	This name pair has sufficient orthographic and phonetic differences.
7.	Alesse	56	The names start with different letters (E vs. A). Elcys has a downstroke letter 'y' in its suffix which is absent in Alesse, providing some orthographic differences. The second syllable ('cys' vs. 'esse') provide some phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: Dose: The dose of Alesse is 1 tablet by mouth once daily or 'use as directed'. The dose of Elcys is weight-based,

No.	Proposed name: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[i]	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
			depending on patient age and stability. Therefore, there is no overlap in dose. Setting of Use: Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable.
8.	Eliquis	56	The length of the names differs by two letters, which provides some orthographic differences. Eliquis has an additional syllable. The second/third syllable ('cys' vs. 'quis') provide sufficient phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: Strength: Eliquis is available in 2.5 mg and 5 mg tablets. The strength/dose of Eliquis will be specified on a prescription/medication order. Elcys is

No.	Proposed name: Elcys Established name: cysteine hydrochloride Dosage form: injection Strength(s): 500 mg/10 mL (50 mg/mL)[b] Usual Dose: 5 or 15 mg cysteine/gram of amino acid[i]	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
			available in a single strength (500 mg/10 mL [50 mg/mL]), which does not overlap with that of Eliquis. Setting of Use: Elcys will be used as an additive in TPN solutions, which in clinical practice, is considered a high-alert medication requiring special safeguards in various points of the medication use process to reduce the risk of error. Furthermore, additives for TPN solutions are typically ordered by the established name (e.g., cysteine) using a TPN prescription/ order program and it is not anticipated that Elcys will be written on a medication order alone. Additionally, there are compatibility considerations with TPN solutions. Therefore, in this scenario, due to the above-mentioned factors, we find this name pair acceptable.
9.	Colcrys	56	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 (%)
10.	Arcet	50
11.	Artiss	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
12.	Acys-5	65	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
13.	Elase	61	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion8F[j].

No.	Name	POCA Score (%)
14.	Selseb	62
15.	Calcet	58
16.	Delsym	58
17.	Losec	58
18.	Ultec	58
19.	Altace	56
20.	Cellcept	56
21.	Gel-Syn	56
22.	Glyset	56
23.	Selsun	56
24.	Velosef	56
25.	Velosef '125'	56
26.	Velosef '250'	56
27.	Velosef '500'	56

[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

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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)

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Date of This Review:	October 10, 2017
Application Type and Number:	NDA 210660
Product Name and Strength:	(b) (4) (L-cysteine hydrochloride) injection 50 mg/mL
Total Product Strength:	500 mg/10 mL
Product Type:	Single-Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Exela Pharma Sciences, LLC
Panorama #:	2017-16394840
DMEPA Primary Reviewer:	Matthew Barlow, RN, BSN
DMEPA Team Leader:	Sarah K. Vee, PharmD

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