CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201848Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
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 7, 2023
Application Type and Number:	NDA 201848
Product Name and Strength:	Hepzato (melphalan (b) (4)) for injection, vial packaged with Delcath Hepatic Delivery System (HDS)]
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Delcath Systems, Inc. (Delcath)
PNR ID #:	2023-1044725235
DMEPA 2 Safety Evaluator:	Ngoc-Linh Do, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Hepzato, 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. Delcath did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Delcath previously submitted the proposed proprietary name, [(b) (4)]***, under IND 032617 on November 3, 2011. However, we found the name, [(b) (4)]*** unacceptable due to misbranding concerns on December 20, 2011 (OSE Record #: 2011-4366).[a]

Subsequently, Delcath submitted the proposed proprietary name, Melblez [(b) (4)]*** on August 31, 2012 under NDA 201848. DMEPA and the Division of Oncology Products 2 (DOP2) held a teleconference with the Applicant to discuss safety issues with the modifier [(b) (4)] on November 7, 2012 (OSE Record #: 2012-2071).[b] As a result of the teleconference, the Applicant withdrew the name, Melblez [(b) (4)]***, in a letter dated November 16, 2012.

Accordingly, Delcath submitted the proposed proprietary name, Melblez Kit***, under NDA 201848 on December 4, 2012. The name was found conditionally acceptable on February 25, 2013 (OSE Record #: 2012-2928).[c] However, NDA 201848 received a complete response on September 12, 2013, and Delcath withdrew the proposed proprietary name, Melblez Kit***, under NDA 201848 on May 1, 2020.

On March 18, 2020 under IND 032617, Delcath submitted the proposed proprietary name Hepzato Kit*** for review. Hepzato Kit*** was found conditionally acceptable on September 4, 2020 (OSE Record #: 2020-38568888).[d]

On February 14, 2023, Delcath submitted a Class 2 Resubmission of the NDA in response to the Complete Response Letter and concurrently submitted a request for proprietary name review (PNR) of Hepzato Kit***. The proprietary name was found conditionally acceptable on May 12, 2023[e].

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[a] Schlick, J. Proprietary Name Review for [(b) (4)] (IND 032617). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 DEC 20. OSE Record #: 2011-4366.

[b] Fahnbulleh, F. Proprietary Name Review Teleconference Memorandum for Melblez [(b) (4)] (Melphalan, NDA 201848). Silver Spring (MD): FDA, CDER, OND, DMEPA & DOP2 (US); 2012 NOV 7. OSE Record #: 2012-2071.

[c] Schlick, J. Proprietary Name Review for Melblez Kit (NDA 201848). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 FEB 25. OSE Record #: 2012-2928.

[d] Thomas, S. Proprietary Name Review for Hepzato Kit (IND 032617). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2020 SEP 3. OSE Record #. 2020-38568888.

[e] Do, N. Proprietary Name Review for Hepzato Kit (NDA 201848). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 MAY 12. OSE Record #. 2023-1044724998.

On June 28, 2023, in collaboration with the Division of Oncology 3 (DO3), a teleconference was held with Delcath to discuss our current thinking regarding the use of two Proprietary names, Hepzato Kit*** and Hepzato*** for NDA 201848. We explained that, while we agree with the proprietary name, Hepzato Kit*** is acceptable when referring to the combination product consisting of a drug component and device components (i.e., Delcath Hepatic Delivery System (HDS)) as one single package, we determined that adding a second proprietary name, Hepzato***, will help distinguish the drug component from the rest of the components within the kit and when referencing the drug component only throughout labels and labeling (i.e., Prescribing Information). Furthermore, upon our review of the intend-to-market samples sent by the company, we note that the container label for the drug component contained the name "Hepzato" whereas the carton labeling that holds the drug component and HDS contained the name "Hepzato Kit***". We asked the company to submit a Request for Proprietary Name Review for the name, Hepzato***, to be used for the drug component. Thus, Delcath submitted the name, Hepzato, for review on June 29, 2023 under NDA 201848.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on June 29, 2023.

- Intended Pronunciation: hep-ZAT-oh KIT
- Active Ingredient: melphalan hydrochloride
- Indication of Use: Treatment of patients with unresectable hepatic-dominant metastatic ocular melanoma (mOM) (b) (4) .
- Route of Administration: intrahepatic arterial infusion via the Delcath Hepatic Delivery System (HDS)
- Dosage Form: for injection
- Strength: 50 mg/vial
- Dose and Frequency: The proposed usual dose is 3 mg/kg ideal body weight (IBW) infused over 30 minutes via the Delcath Hepatic Delivery System (HDS) every 6-8 weeks until progression or up to 6 cycles. The maximum dose to be delivered with the Delcath Hepatic Delivery System is 220 mg per treatment.
- How Supplied: Supplied as a drug/device combination product shipped in a single outer carton with 2 inner cartons which contain:
    - Melphalan hydrochloride for Injection is supplied as a sterile, nonpyrogenic, freeze-dried powder in a carton containing five single-use glass vials each containing 50 mg of lyophilized melphalan (b) (4) and five single use, glass vials each containing 10 mL of diluent.
    - The Delcath Hepatic Delivery System (HDS): a closed circuit of catheters and filters utilized to deliver melphalan hydrochloride.
- Storage: 20° to 25°C and protect from light.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Hepzato would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Hepzato. The Division of Oncology 3 (DO3) did not comment on the findings of OPDP's assessment for Hepzato.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Delcath did not provide a derivation or intended meaning for the proposed proprietary name, Hepzato, 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 can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On August 1, 2023, the Division of Oncology 3 (DO3) did not forward any comments or concerns relating to Hepzato at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy-nine (79) practitioners participated in DMEPA's prescription studies for Hepzato. 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 prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

We had recently searched POCA on March 1, 2023 for "Hepzato" and "Hepzato Kit" when evaluating the proposed proprietary name Hepzato Kit***[g], thus, a POCA search was not repeated in this review.

2.2.6 Communication of DMEPA's Determination

On August 7, 2023, DMEPA 2 communicated our determination to the Division of Oncology 3 (DO3).

3 CONCLUSION

The proposed proprietary name, Hepzato, is conditionally acceptable.

If you have any questions or need clarifications, please contact Latonia Ford, OSE project manager, at 301-796-4901.

3.1 COMMENTS TO DELCATH SYSTEMS, INC. (DELCATH)

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

If any of the proposed product characteristics as stated in your submission, received on June 29, 2023, are altered prior to approval of the marketing application, the name must be resubmitted for review.

[g] Do, N. Proprietary Name Review for Hepzato Kit (NDA 201848). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 MAY 12. OSE Record #. 2023-1044724998.

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. [h]

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
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.

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

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, Cerner RxNorm, 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

[i] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary

POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.

- Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact

the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

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

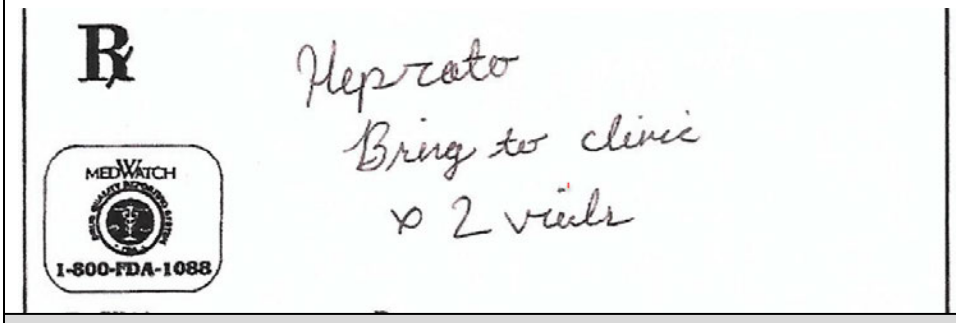
<table>
<tr><td>Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping 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. Hepzato Study (Conducted on July 5, 2023)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order: Hepzato 3mg/kg infusion over 30 minutes via Decath Depatic Delivery System	Hepzato Bring to clinic #2 vials
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Hepzato	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Hepzato

254 People Received Study

79 People Responded

Total	19	22	16	22	79
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
HEPRATO	0	20	0	0	20
HEPROTO	0	2	0	0	2
HEPZATO	19	0	9	22	50
HEPZETO	0	0	1	0	1
PEPZADO	0	0	1	0	1
PEPZATO	0	0	4	0	4
PEPZETO	0	0	1	0	1

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
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Center for Drug Evaluation and Research (CDER)

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Date of This Review:	May 12, 2023
Application Type and Number:	NDA 201848
Product Name and Strength:	Hepzato Kit (melphalan hydrochloride) for injection, 50 mg/vial, [packaged with Delcath Hepatic Delivery System (HDS)]
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Delcath Systems, Inc. (Delcath)
PNR ID #:	2023-1044724998
DMEPA 2 Safety Evaluator:	Ngoc-Linh Do, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD
DMEPA 2 Director:	Danielle Harris, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Hepzato Kit, 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. Delcath submitted an external name study, conducted by [redacted] (b) (4) for this proposed proprietary name. The submitted external name study was previously reviewed under IND 032617 (see Section 1.1 below).

1.1 REGULATORY HISTORY

Delcath previously submitted the proposed proprietary name, [redacted] (b) (4) ***, under IND 032617 on November 3, 2011. However, we found the name, [redacted] (b) (4) *** unacceptable due to misbranding concerns on December 20, 2011 (OSE Record #: 2011-4366).[a]

Subsequently, Delcath submitted the proposed proprietary name, Melblez [redacted] (b) (4) *** on August 31, 2012 under NDA 201848. DMEPA and the Division of Oncology Products 2 (DOP2) held a teleconference with the Applicant to discuss safety issues with the modifier [redacted] (b) (4) on November 7, 2012 (OSE Record #: 2012-2071).[b] As a result of the teleconference, the Applicant withdrew the name, Melblez [redacted] (b) (4) ***, in a letter dated November 16, 2012.

Accordingly, Delcath submitted the proposed proprietary name, Melblez Kit***, under NDA 201848 on December 4, 2012. The name was found conditionally acceptable on February 25, 2013 (OSE Record #: 2012-2928).[c] However, NDA 201848 received a complete response on September 12, 2013, and Delcath withdrew the proposed proprietary name, Melblez Kit***, under NDA 201848 on May 1, 2020.

On March 18, 2020 under IND 032617, Delcath submitted the proposed proprietary name Hepzato Kit for review. Hepzato Kit was found conditionally acceptable on September 4, 2020 (OSE Record #: 2020-38568888).[d]

Thus, Delcath submitted a Class 2 Resubmission of the NDA on February 14, 2023 in response to the Complete Response Letter and concurrently submitted a request for proprietary name review of Hepzato Kit, which is the subject of this review.

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[a] Schlick, J. Proprietary Name Review for [redacted] (b) (4) (IND 032617). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2011 DEC 20. OSE Record #: 2011-4366.

[b] b Fahnbulleh, F. Proprietary Name Review Teleconference Memorandum for Melblez [redacted] (b) (4) (Melphalan, NDA 201848). Silver Spring (MD): FDA, CDER, OND, DMEPA & DOP2 (US); 2012 NOV 7. OSE Record #: 2012-2071.

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[d] Thomas, Sarah. Proprietary Name Review for Hepzato Kit (IND 032617). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2020 SEP 3. OSE Record #. 2020-38568888.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 14, 2023 and the prescribing information received on February 14, 2023.

- Intended Pronunciation: hep-ZAT-oh KIT
- Active Ingredient: melphalan hydrochloride
- Indication of Use: Treatment of patients with unresectable hepatic-dominant metastatic ocular melanoma (mOM) (b) (4)
- Route of Administration: intrahepatic arterial infusion via the Delcath Hepatic Delivery System (HDS)
- Dosage Form: for injection
- Strength: 50 mg/vial
- Dose and Frequency: The proposed usual dose is 3 mg/kg ideal body weight (IBW) infused over 30 minutes via the Delcath Hepatic Delivery System (HDS) every 6-8 weeks until progression or up to 6 cycles. The maximum dose to be delivered with the Delcath Hepatic Delivery System is 220 mg per treatment.
- How Supplied: Supplied as a drug/device combination product shipped in a single outer carton with 2 inner cartons which contain:
    - Melphalan hydrochloride for Injection is supplied as a sterile, nonpyrogenic, freeze-dried powder in a carton containing five single-use glass vials each containing 50 mg of lyophilized melphalan as a hydrochloride salt and five single use, glass vials each containing 10 mL of diluent.
    - The Delcath Hepatic Delivery System (HDS): a closed circuit of catheters and filters utilized to deliver melphalan hydrochloride.
- Storage: 20° to 25°C and protect from light.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Hepzato Kit would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Hepzato Kit. The Division of Oncology 3 (DO3) did not comment on the findings of OPDP's assessment for Hepzato Kit.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Delcath did not provide a derivation or intended meaning for the proposed proprietary name, Hepzato Kit, in their submission. This proprietary name is comprised of multiple words that does not contain any components (i.e., a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On March 31, 2023, the Division of Oncology 3 (DO3) did not forward any comments or concerns relating to Hepzato Kit at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Ninety (90) practitioners participated in DMEPA's prescription studies for Hepzato Kit. 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 prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[f] identified forty-eight (48) names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified four (4) names not previously analyzed. 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. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

[e] USAN stem search conducted on April 15, 2023.

[f] POCA search conducted on March 1, 2023 in version 5.2.

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%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	4
Low similarity name pair: combined match percentage score ≤54%	0

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

Our analysis of the four (4) names contained in Table 1 determined none of the names will pose a risk for confusion with Hepzato Kit as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On May 12, 2023, DMEPA 2 communicated our determination to the Division of Oncology 3 (DO3).

3 CONCLUSION

The proposed proprietary name, Hepzato Kit, is conditionally acceptable.

If you have any questions or need clarifications, please contact Latonia Ford, OSE project manager, at 301-796-4901.

3.1 COMMENTS TO DELCATH SYSTEMS, INC. (DELCATH)

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

If any of the proposed product characteristics as stated in your submission, received on February 14, 2023 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. [g]

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

***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, Cerner RxNorm, 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[h]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

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

a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

   Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

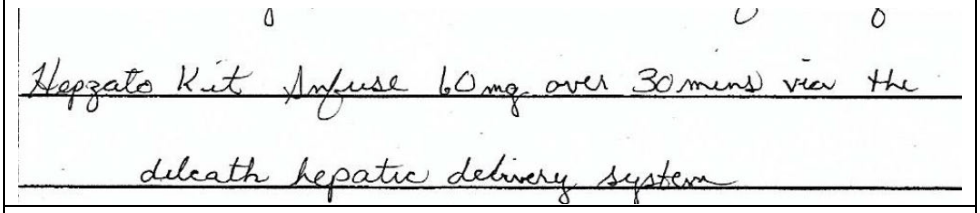
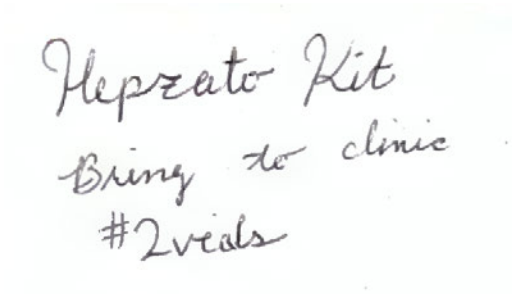
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length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

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

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Hepzato Kit Study (Conducted on March 3, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Hepzato Kit Bring to clinic. #2 vials
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Hepzato Kit	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Hepzato Kit

257 People Received Study

90 People Responded

Total	22	26	18	24	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
HAPZATO	1	0	0	0	1
HAPZATO KIT	1	0	0	0	1
HEPAZATO KIT	1	0	0	0	1
HEPRATO	0	0	0	2	2
HEPRATO KIT	0	0	0	7	7
HEPSATO KIT	0	0	1	0	1
HEPZADO KIT	0	0	11	0	11
HEPZADOKIT	0	0	1	0	1
HEPZATO	2	0	0	1	3
HEPZATO KIT	17	26	2	13	58
ILEPZATO KIT	0	0	0	1	1
PEPZADO KIT	0	0	3	0	3

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

No.	**Proposed name:** Hepzato Kit **Established name:** melphalan hydrochloride **Dosage form:** for injection **Strength(s):** 50 mg/vial **Usual Dose:** 3 mg/kg ideal body weight (IBW) infused over 30 minutes via the Delcath Hepatic Delivery System (HDS) every 6-8 weeks until progression or up to 6 cycles	**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 (%)
1.	Camcevi Kit	55
2.	Hepagam Bt	56

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:** Hepzato Kit **Established name:** melphalan hydrochloride **Dosage form:** for injection **Strength(s):** 50 mg/vial **Usual Dose:** 3 mg/kg ideal body weight (IBW) infused over 30 minutes via the Delcath Hepatic Delivery System (HDS) every 6-8 weeks until progression or up to 6 cycles	**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**
	N/A		

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
1.	Hexapeptide-49	58	Name not in RxNorm database. Unable to find product characteristics in commonly used drug databases.
2.	Hexapeptide-9	58	Name not 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 confusion[i].

No.	Name	POCA Score (%)
	N/A	

[i] 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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DANIELLE M HARRIS
05/12/2023 03:50:10 PM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	February 25, 2013
Reviewer:	James Schlick, RPh, MBA Division of Medication Error Prevention and Analysis
Team Leader:	Todd Bridges, RPh Division of Medication Error Prevention and Analysis
Deputy Director:	Kellie Taylor, Pharm.D, MPH Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Melblez Kit [Melblez (Melphalan) for Injection for use with the Delcath Hepatic Delivery System] 50 mg
Application Type/Number:	NDA 201848
Applicant:	Delcath Systems, Inc.
OSE RCM #:	2012-2928

*** This document contains proprietary and confidential information that should not be released to the public.***

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Melblez Kit, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A, respectively.

1.1 REGULATORY HISTORY

The proposed proprietary name, [redacted] (b) (4) was found unacceptable by DMEPA in OSE 2011-4366, dated December 20, 2011, under IND 032617. Subsequently, the Applicant submitted the name Melblez [redacted] (b) (4) under NDA 201848 dated August 31, 2012. DMEPA and the Division of Oncology Products 2 (DOP2) held a teleconference with the Applicant to discuss safety issues with the modifier [redacted] (b) (4) on November 7, 2012. As a result of the teleconference, the Applicant withdrew the name, Melblez [redacted] (b) (4), in a letter dated November 16, 2012 and submitted an alternate name, Melblez Kit, under this NDA. The proprietary name request submitted on December 4, 2012 is the subject of this review.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 4, 2012 proprietary name submission.

- Active Ingredient: Melphalan
- Indication of Use: Treatment of patients with unresectable metastatic ocular melanoma in the liver.
- Route of Administration: Percutaneous hepatic artery infusion with the Delcath Hepatic Delivery System
- Dosage Form: Powder for Injection
- Strength: 50 mg/vial (same as currently marketed melphalan products)
- Dose and Frequency: 3 mg/kg of ideal body weight (IBW) once every [redacted] (b) (4) weeks for up to six cycles
- How Supplied: Supplied as a drug/device combination product shipped in a single outer carton with two inner cartons. Melphalan and the diluent for melphalan are located in one carton. This carton supplies melphalan as a sterile, non-pyrogenic, freeze-dried powder containing five (5) single-use vials and five (5) single-use, vials containing diluent. The other carton contains the supplies that comprise the Delcath Hepatic Delivery System.
- Storage: Store at 20ºC to 25 ºC
- Container and Closure Systems: Container and closure system consists of USP [redacted] (b) (4) clear tubular glass vials, closed with rubber stopper, and sealed with aluminum seal with flip-off caps.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Oncology Products 2 (DOP2) concurred with the findings of OPDP's promotional 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

The December 18, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Melblez Kit, was not created to convey any particular meaning. The proposed name is comprised of multiple words that contain two components: 1) the proposed root name, Melblez, and 2) the modifier, Kit. Because it is not uncommon for prescribers to drop the modifier component of a name, DMEPA considers the name 'Melblez Kit' and 'Melblez' in our analysis.

Modifier "Kit"

In a teleconference on November 7, 2012, DMEPA recommended the Applicant consider naming the proposed product using a proprietary name in conjunction with the modifier "kit". The use of the modifier, kit, will help alert health care practitioners that the product consists of the drug and the components used to prepare and administer the drug.

We assessed the modifier, kit, prior to the teleconference to determine if it could cause confusion as a result of being associated with a particular class of drugs or route of administration. The results of a search at Drugs@FDA for proprietary names containing the modifier "kit' (see Appendix F) indicated that use of the modifier "kit" in proprietary names is not limited to any particular drug classes or routes of administration. Additionally, the results of the search indicate that the modifier, kit, is used to convey a product with multiple components used to prepare and administer the drug.

2.2.3 Medication Error Data Selection of Cases

DMEPA searched the FAERS database for medication errors involving melphalan which would be relevant for this review.

The January 22, 2013 search of the FDA Adverse Event Reporting System (FAERS) database used the following search terms: active ingredient "Melphalan", and verbatim term "Melpha*". The reaction terms used were the MedDRA High Level Group term

(HLGT) “Medication Errors”; High Level terms (HLT) “Product Packaging Issues”, “Product Label Issues”, and “Product Quality Issues (NEC). The search time frame was open ended.

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

After individual review, 15 reports were not included in the final analysis for the following reasons:

- Medication error from concomitant drugs, not related to melphalan (n=9)
- Drug product quality issues not related to melphalan (n=2)
- Adverse event related to melphalan, not related to a medication error (n=4)

This left 13 cases for review. However, none of the 13 medication error cases were related to name confusion and, thus, are not relevant to this review. (See Appendix G for case numbers).

2.2.4 FDA Name Simulation Studies

Eighty-two practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Nineteen participants responded correctly. Nineteen other participants correctly interpreted the letter string ‘Melb’, but misinterpreted the letter string ‘lez’ as ‘liss’ or ‘liz’. Seven participants misinterpreted the letter string ‘Melb’ as ‘Mebl’. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE January 3, 2013 e-mail, the Division of Oncology Products 2 (DOP2) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Melblez Kit. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Melblez Kit, identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Tables 1 also includes the names identified from the FDA Prescription Simulation or by (b) (4) not identified by DMEPA, and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)					
Look Similar to Melblez					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Multi-Day	FDA	Maldec	FDA	Marblen	FDA
Melfiat	FDA	Melbex***	FDA	Mellaril	FDA
(b) (4)***	FDA	Methadex	FDA	Milkinol	FDA
Miltex	FDA	Mobic	External	Multaq	FDA
Multidex	FDA	Multilex	FDA	Naftin	FDA
Nalbuphine	External	Naldec	FDA	Nalfon	FDA
Northyx	FDA	Nulojix	FDA	(b) (4)***	FDA
Wellbid D	FDA	Zaltrap	FDA	Zelboraf	FDA
Amabelz***	FDA	Mebaral	FDA	Mollifene	FDA
Milantex	FDA	Nolvadex	FDA	Naldelate	FDA
Look and Sound Similar to Melblez					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Melblez***	FDA	Melphalan	Both	(b) (4)***	Both
Velban	FDA				
Look Similar to Melblez Kit					
Marqibo Kit	FDA	Helidac	FDA		

Our analysis of the 36 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 36 names will not pose a risk for confusion as described in Appendices D through E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Oncology Products 2 via e-mail on February 1, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Oncology Products 2 on February 12, 2013, they stated no additional concerns with the proposed proprietary name, Melblez Kit.

*** This document contains proprietary and confidential information that should not be released to the public.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have questions or need clarifications, please contact Sue Kang, OSE project manager, at 301-796-4216.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Melblez Kit, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your December 4, 2012 submission are altered, the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 REFERENCES

1. ***Micromedex Integrated Index (http://csi.micromedex.com)***

   Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

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

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)***

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

   DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. ***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.

6. ***Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)***

   Drugs@FDA contains most of the drug products approved 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. ***U.S. Patent and Trademark Office (http://www.uspto.gov)***

   USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)***

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. ***Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)***

   The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

10. ***Natural Medicines Comprehensive Databases (www.naturaldatabase.com)***

    Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

11. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

13. ***Red Book (www.thomsonhc.com/home/dispatch)***

    Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

14. ***Lexi-Comp (www.lexi.com)***

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

15. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

16. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

18. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. ***Dogpile (www.dogpile.com)***

    Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

20. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). 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. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

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.

4. 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.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[3] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

[3] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

Moreover, DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

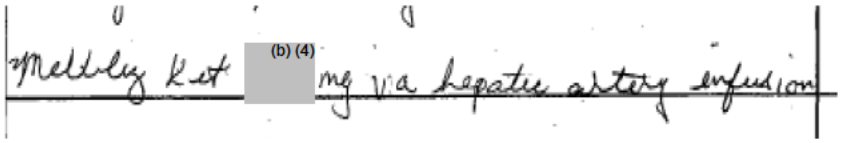
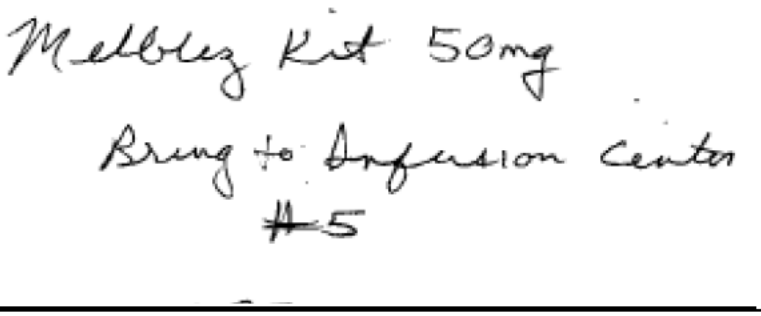
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Melblez Kit	Scripted May Appear as	Spoken May Be Interpreted as
M	ss, W, N, V	
m	rn, nn, n, v, w, wi, vi, onc, z	
e	a, i, l, o, u,p	Any vowel
l	B,e, s, A, P, i	
b	l, h, k	p,v,d
z	c, e, g, n, m, q, r, s, v	c,s,x
K	R, X	C, Qu, Que, Ques, Q
k	x, h, la	c,g
i	e,l	y
t	r, f, x, A,z	d
Letter strings		
Mel	Hel, Mil,Mul, Naf, Zal, Mol	
Melb	Mobl, Velb, Mald, Marbl, Melf, Mell, Nalf, Wellb, Zelb	Mobl, Velb
Blez	belz	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Melblez Kit Study (Conducted on Dec 31, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: 	Melblez Kit 50 mg Disp #5 Bring to Infusion Center
Outpatient Prescription: 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

191 People Received Study
82 People Responded

Study Name: **Melblez Kit**

Total	27	29	26	82
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
MALBLESS KIT	0	1	0	1
MALBLEST KIDS (OR KITS)	0	1	0	1
MALPLESS	0	1	0	1
MEBBLEG KIT	2	0	0	2
MEBBLIZ KIT	1	0	0	1
MEBBLY	1	0	0	1
MEBBLY KIT	2	0	0	2
MEBLEZ KIT	0	0	1	1
MEBLIZ KIT	0	0	1	1
MELBILZ KIT	1	0	0	1
MELBIS KIDS	0	1	0	1
MELBISKIS	0	1	0	1
MELBLED KIDS	0	1	0	1
MELBLEG KIT	3	0	0	3
MELBLES	0	1	0	1
MELBLESS KIT	0	3	0	3

MELBLET KIT	0	1	0	1
MELBLETH KIT	0	1	0	1
MELBLEZ	0	0	1	1
MELBLEZ KIT	2	1	14	17
MELBLEZ KIT 50 MG	0	0	1	1
MELBLIG KIT	3	0	0	3
MELBLIQ KIT	1	0	0	1
MELBLIS KIT	0	1	0	1
MELBLISS	0	1	0	1
MELBLISS KIT	0	8	0	8
MELBLISS KITS	0	3	0	3
MELBLIZ KIT	0	1	7	8
MELBLUZ KIT	0	0	1	1
MELBLY	1	0	0	1
MELBLY KET	1	0	0	1
MELBLY KIT	5	0	0	5
MELBY K	1	0	0	1
MELLILY	1	0	0	1
MELTILIG KIT	1	0	0	1
MELXILY KIT	1	0	0	1
NOBLESSE KITS	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Melblez Kit	Failure preventions
1.	Methadex	Dexamethasone/Neomycin Sulfate/Polymixin B Sulfate	Look similar	The pair has sufficient orthographic differences
2.	Milkinol	Mineral Oil	Look similar	The pair has sufficient orthographic differences
3.	Mobic	Meloxicam	Look similar	The pair has sufficient orthographic differences
4.	Multidex	Maltodextrin	Look similar	The pair has sufficient orthographic differences
5.	Multilex	Multivitamin Nutritional Supplement	Look similar	The pair has sufficient orthographic differences
6.		Nalbuphine	Look similar	The pair has sufficient orthographic differences
7.	Northyx	Methimazole	Look similar	The pair has sufficient orthographic differences
8.	Nulojix	Belatacept	Look similar	The pair has sufficient orthographic differences
9.	(b) (4) ***	Ferumoxytol	Look similar	The pair has sufficient orthographic differences
10.	Melblez***	Melphalan	Look and sound similar	Name that is the subject of this review
11.	(b) (4)			
12.	Naldec	Chlorpheniramine/ Phenylpropanolamine/ Phenylephrine/ Phenyltoloxamine	Look similar	Name identified in Red Book database. Unable to find product characteristics in commonly used drug databases.
13.	Mebaral	Mephobarbital	Looks similar	The pair has sufficient orthographic differences
14.	Naldelate	Chlorpheniramine/ Phenylpropanolamine/ Phenylephrine/ Phenyltoloxamine	Looks similar	The pair has sufficient orthographic differences

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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.	(b) (4)		

*** This document contains proprietary and confidential information that should not be released to the public.

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
2.	(b) (4)		
3.	Helidac (Bismuth Subsalicylate/ Metronidazole/ Tetracycline) Kit for Therapy Bismuth Subsalicylate: 262 mg Metronidazole: 250 mg Tetracycline: 500 mg Usual Dose: Take (b) (4) capsules by mouth four times daily for 14 days	Orthographic Similarity with Melblez Kit: The letter string 'Hel' can look similar to the letter string 'Mel' when scripted. The letter string 'ac' can look similar to the letter string 'ez' if there is no downstroke in the letter 'z'. Both names contain the modifier "kit".	Orthographic Difference with Melblez Kit: The letter 'i' in Helidac separates the two upstroke letters 'l' and 'd'. The name Melblez has three upstroke letters together in the name. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Four times daily vs. every four weeks

*** This document contains proprietary and confidential information that should not be released to the public.

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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.	Maldec (Carbinoxamine / Pseudoephedrine) Oral Syrup 4 mg/60 mg per 5 mL Usual Dose: 5 mL to 10 mL by mouth four times daily as needed	Orthographic Similarity with Melblez: The letter string 'Mald' can look similar to the letter string 'Melb' when scripted. The letter string 'ec' can look similar to the letter 'ez' if the letter 'z' is scripted without the downstroke.	Orthographic Difference with Melblez: The name Melblez has an additional upstroke letter 'l' in the name where Maldec does not. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Four times daily as needed vs. every four weeks
5.	Marblen (Calcium Carbonate/ Magnesium Carbonate) Oral Suspension 520 mg/400 mg per 5 mL Usual Dose: 5 mL to 10 mL by mouth with meals and at bedtime	Orthographic Similarity with Melblez: The letter string 'Marbl' can look similar to the letter string 'Melb' when scripted. The letter string 'en' can look similar to the letter string 'ez' if the letter 'z' is scripted without the downstroke.	Orthographic Difference with Melblez: The name Melblez has an additional upstroke letter 'l' in the name where Marblen does not. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: With meals and at bedtime vs. every four weeks

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
6.	Melfiat (Phendimetrazine) Extended-release Capsules 105 mg Usual Dose: 1 tablet by mouth once daily	Orthographic Similarity with Melblez: The letter string 'Melfi' can look similar to the letter string 'Melbi' when scripted if the letter 'l' in Melblez is truncated to look similar to the letter 'i'. If the letter 'z' is scripted with a cross stroke, both names have a cross stroke letter at the end of the name.	Orthographic Difference with Melblez: The letter 'a' in Melfiat does not look similar to the second letter 'e' in Melblez when scripted. The modifier "kit" adds an orthographic difference when included. Dose and Strength: There is no overlap or numerical similarity. Frequency of Administration: Once daily vs. every four weeks
7.	Mellaril (Thioridazine) Tablets 10 mg, 25 mg, 50 mg, 100 mg, and 200 mg Off market, but generics exist Usual Dose: 10 mg to 100 mg by mouth three times daily	Orthographic Similarity with Melblez: The letter string 'Mell' can look similar to the letter string 'Melb' when scripted. Strength: Both products have a 50 mg strength	Orthographic Difference with Melblez: The name Melblez has an additional upstroke letter 'b' between the letters 'l' where Mellaril does not. The letter string 'aril' does not look similar to the letter string 'ez' when scripted. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Three times daily vs. every four weeks

No.	**Proposed name: Melblez Kit** **Dosage Form: Powder for Injection** **Strength: 50 mg (5 mg/mL when reconstituted)** **Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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.	(b) (4) (Miltefosine) Tablets or Capsules Usual Dose: 50 mg to 100 mg by mouth once daily	Orthographic Similarity with Melblez: The letter string '(b) (4)' can look similar to the letter string 'Mel'. The letter string '(b) (4)' can look similar to the letter string 'ez' (b) (4) Strength: Based on the usual dose, Miltex may have a 50 mg strength that would overlap with Melblez (b) (4).	Orthographic Difference with Melblez: The name Melblez has the letter string 'bl', two upstroke letters after the first 'l', where (b) (4) has one cross stroke letter (b) (4) The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Once daily vs. every four weeks
9.	Multaq (Dronedarone) Tablets 400 mg Usual Dose: 1 tablet by mouth twice daily	Orthographic Similarity with Melblez: 'The letter string 'Mul' can look similar to the letter string 'Mel' when scripted. The letter string 'aq' can look similar to the letter string 'ez' if the letter 'z' is scripted with a downstroke.	Orthographic Difference with Melblez: The name Melblez has the letter string 'bl', two upstroke letters after the first 'l', where Multaq has one cross stroke letter 't' after the 'l'. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Twice daily vs. every four weeks

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
10.	Naftin (Naftifine) Topical Cream and Gel Cream: 1% and 2% Gel: 1% Usual Dose: Apply as directed to the skin twice daily	Orthographic Similarity with Melblez: The letter string 'Naf' can look similar to the letter string 'Mel' when scripted. The letter string 'in' can look similar to the letter string 'ez' if the letter 'z' is scripted without the downstroke.	Orthographic Difference with Melblez: The name Melblez has the letter string 'bl', two upstroke letters after the first 'l', where Naftin has one cross stroke letter 't' after the 'f'. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Twice daily vs. every four weeks
11.	Nalfon (Fenoprofen) Tablets 600 mg Off market, but generics exist Usual Dose: 1 tablet by mouth three to four times daily	Orthographic Similarity with Melblez: The letter string 'Nalf' can look similar to the letter string 'Melb' when scripted. The letter string 'on' can look similar to the letter string 'ez' if the letter 'z' is scripted without the downstroke.	Orthographic Difference with Melblez: The name Melblez has a third upstroke letter 'l' in the middle of the name where Nalfon does not. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Three to four times daily vs. every four weeks

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
12.	Wellbid D (Guaifenesin/ Phenylephrine) Sustained-release Tablets 600 mg/40 mg and 1200 mg/40 mg Usual Dose: 1 tablet every 12 hours	Orthographic Similarity with Melblez: The letter string 'Wellb' can look similar to the letter string 'Melb' when scripted.	Orthographic Difference with Melblez: The letter string 'id' does not look similar to the letter string 'ez' when scripted. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Twice daily vs. every four weeks
13.	Zelboraf (Vemurafenib) Tablet 240 mg Usual Dose: 2 to 4 tablets by mouth every 12 hours	Orthographic Similarity with Melblez: The letter string 'Zelb' can look similar to the letter string 'Melb' when scripted. If the letter 'z' in Melblez is scripted with a downstroke, both names have a downstroke letter at the end of the name. Setting of Use: Both products are used in the oncology setting	Orthographic Difference with Melblez: The name Melblez has a third upstroke letter 'l' in the middle of the name where Zelboraf does not. The letter string 'ora' does not look similar to the second letter 'e' in Melblez. The modifier "kit" adds an orthographic difference when included. Dose: There is no overlap or numerical similarity in dose. Frequency of Administration: Twice daily vs. every four weeks

No.	**Proposed name: Melblez Kit** **Dosage Form: Powder for Injection** **Strength: 50 mg (5 mg/mL when reconstituted)** **Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
14.	Velban (Vinblastine) Injection 1 mg/mL Usual Dose: 4 mg/m^2 to 6 mg/m^2 intravenously once every week to every three weeks.	Orthographic Similarity with Melblez: The letter string 'Velb' can look similar to the letter string 'Melb' when scripted. The letter string 'an' can look similar to the letter string 'ez' if the letter 'z' is scripted without the downstroke. Phonetic: The letter string 'Velb' is phonetically similar to the letter string 'Melb'. Dosage Form: Both products are for intravenous use Setting of Use: Both products are used in the oncology setting	Orthographic Difference with Melblez: The name Melblez has a third upstroke letter 'l' in the middle of the name where Velban does not. The modifier "kit" adds an orthographic difference when included. Phonetic: The letter string 'an' is not phonetically similar to the letter string 'lez'. The modifier "kit" adds a phonetic difference when included. Dose: There is no overlap or numerical similarity in dose.

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
15.	Melphalan Injection and Tablets Injection: 50 mg Tablets: 2 mg Usual Dose: Tablets: 6 mg by mouth daily for 2 to 3 weeks or 12 mg to 16 mg orally daily for 5 days Intravenous: 16 mg/m^2 every 2 weeks for 4 doses	Orthographic Similarity with Melblez: Both names begin with the letter string 'Mel'. Both names have upstroke letters in similar positions of each name. Phonetic Similarity with Melblez: Both names begin with the letter string 'Mel'. Strength: Both products have a 50 mg strength Numerical Similarity in Dose: Both products can have numerically similar doses based on weight. For example, 25 mg can look similar to 250 mg. Frequency of Administration: Both products can be prescribed as 'give today' or 'give on Day xx' Dosage Form: Both products are the same dosage form Setting of Use: Both products are used in the oncology setting	Orthographic Difference with Melblez: The name Melphalan has a downstroke letter between two upstroke letters where Melblez has three upstroke letters. The letter string 'alan' does not look similar to the letter string 'ez' when scripted. The modifier "kit" adds an orthographic difference when included. Phonetic Difference with Melblez: The letter string 'phalan' is not phonetically similar to the letter string 'blez'. The modifier "kit" adds a phonetic difference when included.

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
16.	Zaltrap (Ziv-Aflibercept) Injection 25 mg/mL Usual Dose: 2 mg/kg or 4 mg/kg intravenously every 2 weeks	Orthographic Similarity with Melblez: The letter string 'Zal' can look similar to the letter string 'Mel' when scripted. If the letter 'z' in Melblez is scripted with a downstroke, both names have a downstroke letter at the end of the name. Dose: There is an overlap in dose based on weight for both products. Dosage Form: Both products are the same dosage form Setting of Use: Both products are used in the oncology setting	Orthographic Differences with Melblez: The name Melblez has the letter string 'bl', two upstroke letters after the first 'l', where Zaltrap has one cross stroke letter 't' after the 'l'. The modifier "kit" adds an orthographic difference when included. Frequency of Administration: Once every two weeks vs. once every 4 weeks
17.	Amabelz*** (Estradiol/Norethindrone Acetate) Tablets 1 mg/0.5 mg 0.5 mg/0.1 mg Usual Dose: 1 tablet orally once daily	Orthographic Similarity with Melblez: Both names have the letter 'm' at or near the beginning of the name. The letter string 'belz' can look similar to the letter string 'blez'.	Orthographic Differences with Melblez: The letter 'A' at the beginning of the name Amabelz provides orthographic differentiation. Melblez has an additional upstroke letter 'l' in the third position where Amabelz does not. The modifier "kit" adds an orthographic difference when included. Dose and Strength: There is no overlap or numerical similarity Frequency of Administration: Once daily vs. every four weeks

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No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
18.	Mollifene (Carbamide Peroxide) Otic Drops 6.5% Usual Dose: Apply 5 to 10 drops to the affected area 4 times per day for up to 4 days	Orthographic Similarity with Melblez: The letter string 'Mol' can look similar to the letter string 'Mel' when scripted. Both names have three upstroke letters in the middle of the name.	Orthographic Differences with Melblez: Mollifene has a letter 'i' between the second and third upstroke letters where Melblez does not. Mollifene has the letter 'e' at the end of the name where Melblez does not. The modifier "kit" adds an orthographic difference when included. Dose and Strength: There is no overlap or numerical similarity Frequency of Administration: Four times a day for up to 4 days vs. every four weeks
19.	Milantex (Aluminum Hydroxide/Magnesium Hydroxide/Simethicone) 200 mg/200 mg/20 mg per 5 mL Usual Dose: 10 mL to 20 mL orally between meals and at bedtime	Orthographic Similarity with Melblez: The letter string 'Mil' can look similar to the letter string 'Mel'. If the letter 'z' in Melblez is scripted with a cross stroke, the letter string 'ez' can look similar to the letter string 'ex' in Milantex.	Orthographic Differences with Melblez: The letter string 'ant' does not look similar to the letter string 'bl'. The modifier "kit" adds an orthographic difference when included. Dose and Strength: There is no overlap or numerical similarity Frequency of Administration: Between meals and at bedtime vs. every four weeks

No.	Proposed name: Melblez Kit Dosage Form: Powder for Injection Strength: 50 mg (5 mg/mL when reconstituted) Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
20.	Nolvadex (Tamoxifen) Tablets 10 mg and 20 mg Usual Dose: 20 mg once daily or 10 mg to 20 mg orally twice daily	Orthographic Similarity with Melblez: The letter string 'Nol' can look similar to the letter string 'Mol'. If the letter 'z' is scripted with a cross stroke, the letter string 'ez' in Melblez can look similar to the letter string 'ex'. Dose: There is numerical similarity with the 20 mg dose and 200 mg dose of Melblez based on weight. Setting of Use: Both products are used in the oncology setting	Orthographic Differences with Melblez: The letter string 'vad' does not look similar to the letter string 'bl'. The modifier "kit" adds an orthographic difference when included. Strength: There is no overlap or numerical similarity Frequency of Administration: Once daily or twice daily vs. every four weeks
21.	Multi-Day (Multivitamin) Tablets Usual Dose: 1 to 2 tablets orally once daily	Orthographic Similarity with Melblez:: The letter string 'Mul' can look similar to the letter string 'Mel'. If the letter 'z' in Melblez is scripted with a downstroke, the letter string 'ez' can look similar to the letter string 'ay'. If no dash is used and the letter 'd' is scripted in lower case, then both names have three upstroke letters in the middle of the name.	Orthographic Differences with Melblez:: There is a cross stroke letter 't' in the fourth position of the name Multi-Day where there is an upstroke letter 'b' in the fourth position in Melblez. The dash and upper case letter 'D' provide orthographic differentiation when scripted. The modifier "kit" adds an orthographic difference when included. Dose and Strength: There is no overlap or numerical similarity Frequency of Administration: Once daily vs. every four weeks

No.	**Proposed name: Melblez Kit** **Dosage Form: Powder for Injection** **Strength: 50 mg (5 mg/mL when reconstituted)** **Usual Dose: 3 mg/kg IBW via HAI every 4 weeks (125 mg to 280 mg)**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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**
22.	Marqibo Kit (Vincristine Liposomal) Injection 5 mg/31 mL when reconstituted Usual Dose: 2.25 mg/m^2 (3.6 mg to 5 mg) intravenously over 1 hour once every 7 days	Orthographic Similarity with Melblez Kit: Both names begin with the letter 'M'. Both names have the word 'Kit' in the name. Frequency of Administration; Both products can be prescribed as 'give today' or 'give on Day xx'	Orthographic Differences with Melblez Kit: The letter string 'arqibo' does not look similar to the letter string 'elblez'. Dose and Strength: There is no overlap or numerical similarity

Appendix F: Results of Search at Drugs@FDA for Proprietary Names Containing the Modifier "Kit"

Drug Name/Active Ingredients
AMERSCAN MDP **KIT** TECHNETIUM TC-99M MEDRONATE **KIT**
ARIDOL **KIT** MANNITOL
BUPIVACAINE HYDROCHLORIDE **KIT** BUPIVACAINE HYDROCHLORIDE
CYANO**KIT** HYDROXOCOBALAMIN
CYSVIEW **KIT** HEXAMINOLEVULINATE HYDROCHLORIDE
DICOPAC **KIT** CYANOCOBALAMIN; CYANOCOBALAMIN CO-57; CYANOCOBALAMIN CO-58
GATTEX **KIT** TEDUGLUTIDE RECOMBINANT
ID**KIT**:HP CITRIC ACID; UREA C-13
IFEX/MESNEX **KIT** IFOSFAMIDE; MESNA
IFOSFAMIDE/MESNA **KIT** IFOSFAMIDE; MESNA
IXEMPRA **KIT** IXABEPILONE
JEVTANA **KIT** CABAZITAXEL
LARYNG-O-JET **KIT** LIDOCAINE HYDROCHLORIDE
LARYNGOTRACHEAL ANESTHESIA **KIT** LIDOCAINE HYDROCHLORIDE
LIDOSITE TOPICAL SYSTEM **KIT** EPINEPHRINE; LIDOCAINE HYDROCHLORIDE
LTA II **KIT** LIDOCAINE HYDROCHLORIDE
LUTREPULSE **KIT** GONADORELIN ACETATE
MARQIBO **KIT** VINCRISTINE SULFATE
MERETEK UBT **KIT** (W/ PRANACTIN) UREA C-13
MPI DTPA **KIT** - CHELATE TECHNETIUM TC-99M PENTETATE **KIT**
NEO TECT **KIT** TECHNETIUM TC-99M DEPREOTIDE
PEDIATRIC LTA **KIT** LIDOCAINE HYDROCHLORIDE
PREVEN EMERGENCY CONTRACEPTIVE **KIT** ETHINYL ESTRADIOL; LEVONORGESTREL
PYTEST **KIT** UREA, C-14
ROCEPHIN **KIT** CEFTRIAXONE SODIUM; LIDOCAINE
RUBRATOPE-57 **KIT** COBALT CHLORIDE CO-57; CYANOCOBALAMIN; CYANOCOBALAMIN CO-57; INTRINSIC FACTOR
RUBRATOPE-60 **KIT** COBALT CHLORIDE CO-60; CYANOCOBALAMIN; CYANOCOBALAMIN CO-60; INTRINSIC FACTOR
SODIUM POLYPHOSPHATE-TIN **KIT** TECHNETIUM TC-99M POLYPHOSPHATE **KIT**
SUPREP BOWEL PREP **KIT** MAGNESIUM SULFATE ANHYDROUS; POTASSIUM SULFATE; SODIUM SULFATE
TECHNESCAN PYP **KIT** TECHNETIUM TC-99M PYROPHOSPHATE **KIT**
TECHNETIUM TC 99M ALBUMIN AGGREGATED**KIT** TECHNETIUM TC-99M ALBUMIN AGGREGATED **KIT**
TECHNETIUM TC 99M DIPHOSPHONATE-TIN **KIT** TECHNETIUM TC-99M ETIDRONATE **KIT**
TECHNETIUM TC-99M PENTETATE **KIT** TECHNETIUM TC-99M PENTETATE **KIT**

Appendix G: List of FAERS Cases

Case	Version
3675064	2
3916099	1
4018829	1
4043159	1
4214097	1
5334924	1
5334991	1
5334995	1
5334999	1
6861101	1
7361708	2
8140344	2
8301867	1

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/s/

JAMES H SCHLICK
02/25/2013

TODD D BRIDGES
02/25/2013

CAROL A HOLQUIST on behalf of KELLIE A TAYLOR
02/27/2013

CAROL A HOLQUIST
02/27/2013