

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**205580Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

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**PROPRIETARY NAME REVIEW**

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

**\*\*\* This document contains proprietary information that cannot be released to the public\*\*\***

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<b>Date of This Review:</b>	March 22, 2018
<b>Application Type and Number:</b>	NDA 205580
<b>Product Name and Strength:</b>	Belrapzo (bendamustine HCL) Injection
<b>Total Product Strength:</b>	100 mg/4 mL (25 mg/mL)
<b>Product Type:</b>	Single Ingredient
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Eagle Pharmaceuticals, Inc.
<b>Panorama #:</b>	2018- 20949012
<b>DMEPA Safety Evaluator:</b>	Idalia E. Rychlik, PharmD.
<b>DMEPA Team Leader:</b>	Hina Mehta, PharmD.
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## 1 INTRODUCTION

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

### 1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 2, 2018.

- Intended Pronunciation: bell-RAP-zoh
- Active Ingredient: bendamustine hydrochloride
- Indication of Use: treatment of chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.
- Route of Administration: intravenous infusion
- Dosage Form: injection
- Strength: 100 mg/4 mL (25 mg/mL)
- Dose and Frequency: The usual dosage and frequency of administration for this product is:
  - CLL: 100 mg/m<sup>2</sup> infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles
  - NHL: 120 mg/m<sup>2</sup> infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles

(b) (4)

- How Supplied: multi-dose vials with an (b) (4) stopper
- Storage: refrigerated (2°C to 8°C), protected from light

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

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

### 2.2 SAFETY ASSESSMENT

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

### **2.2.1 United States Adopted Names (USAN) Search**

There is no USAN stem present in the proprietary name<sup>a</sup>.

### **2.2.2 Components of the Proposed Proprietary Name**

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

### **2.2.3 Comments from Other Review Disciplines at Initial Review**

In response to the OSE, February 22, 2018 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

### **2.2.4 FDA Name Simulation Studies**

Ninety-two (92) practitioners participated in DMEPA's prescription studies. One participant misinterpreted the name Belrapzo as "Darazol" in the voice prescription simulation, which is a close variation to the currently marketed product "Danazol". We note that the name pair have sufficient orthographic and phonetic differences, with a combined POCA score of 40.

Phonetically the first syllables ("Bel-" vs. "Dan") of this name pair provide some phonetic differences. Orthographically, the prefixes (Bel vs. Dan), infixes (rap vs. a), and the presence of an upstroke letter "l" in the suffix of Danazol provide sufficient differences. In addition, Belrapzo and Danazol differ in dosage form (*injection vs. capsule*), routes of administration (*intravenous vs. oral*), and frequency (*once every 21 or 28-day cycle, for a total 6 to 8 cycles vs. 2 to 3 times daily*). We evaluate this name pair in Appendix E.

Appendix B contains the results from the verbal and written prescription studies.

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

Our POCA search<sup>b</sup> identified 34 names with a combined phonetic and orthographic score of  $\geq 55\%$  or an individual phonetic or orthographic score  $\geq 70\%$ . These names are included in Table 1 below.

### **2.2.6 Names Retrieved for Review Organized by Name Pair Similarity**

Table 1 lists the number of names retrieved from our POCA search, FDA Name Simulation Studies and the (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

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<sup>a</sup> USAN stem search conducted on (2/13/18).

<sup>b</sup> POCA search conducted on (2/13/18) in version 4.2.

<b>Table 1. Similarity Category</b>	<b>Number of Names</b>
Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	30
Low similarity name pair: combined match percentage score $\leq 54\%$	5

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

Our analysis of the 36 names contained in Table 1 determined that 35 of the names will not pose a risk for confusion as described in Appendices C through H. However, the proposed name could be confused with another proposed proprietary name, (b) (4) \*\*\* for the reasons described below (see section titled “Belrapzo vs. Perhazo”). Thus, the ultimate acceptability of the proposed proprietary name, Belrapzo is dependent upon which underlying application is approved first. We evaluated the status of the underlying application of the conflicting name, (b) (4) \*\*\* and determined that the application remains in IND status. Therefore, if the proposed proprietary name, Belrapzo, is granted approval under NDA 205580 on or before the March 30, 2018 PDUFA goal date for the application, this application approval will precede approval of the application with the conflicting name, (b) (4) \*\*\*. Based on our assessment, we do not object to the proposed proprietary name, Belrapzo, at this time.

**Belrapzo vs. (b) (4) \*\*\***



(b) (4)

We acknowledge that our conclusion differs from that of the external study conducted by (b) (4). However, the external study did not identify the pending proprietary name as it is not an approved product.

### 2.2.8 Discussion of Dual Proprietary Name

Eagle Pharmaceuticals has proposed two different marketing applications for their bendamustine hydrochloride injection. NDA 208194 was approved on December 7, 2015 under the proprietary name Bendeka. The Applicant now proposes NDA 205580 under the proposed proprietary name Belrapzo. Both products are indicated for treatment of chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen. The products are available in 100 mg/4 mL injection dosage form. However, the preparation instructions for the products differ.

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

<b>Table 2. Comparison of Belrapzo and Bendeka</b>		
<b>Attribute</b>	<b>Belrapzo</b>	<b>Bendeka</b>
<b>Application Number</b>	NDA 205580	NDA 208194
<b>Strength</b>	100 mg/4 mL (25 mg/mL)	100 mg/4 mL (25 mg/mL)
<b>How Supplied</b>	4 mL multi-dose vial	4 mL multi-dose vial
<b>Dosing and Administration</b>	<p>The usual dosage and frequency of administration for this product is:</p> <ul style="list-style-type: none"> <li>CLL: 100 mg/m<sup>2</sup> infused intravenously over <b>30 minutes</b> on days 1 and 2 of a 28-day cycle, up to 6 cycles</li> </ul>	<p>The usual dosage and frequency of administration for this product is:</p> <ul style="list-style-type: none"> <li>CLL: 100 mg/m<sup>2</sup> infused intravenously over <b>10 minutes</b> on days 1 and 2 of a 28-day cycle, up to 6 cycles</li> </ul>

<sup>c</sup> Institute for Safe Medication Practices. Safety briefs: Vitamin D-angerous? ISMP Med Saf Alert Community/Ambulatory Care. 2012; 11(11): 1-4.

<sup>d</sup> Institute for Safe Medication Practices. Safety Briefs: On the watch. ISMP Med Saf Alert Acute Care. 2006; 11(2):1.

	<ul style="list-style-type: none"> <li>NHL: 120 mg/m<sup>2</sup> infused intravenously over <b>60 minutes</b> on days 1 and 2 of a 21-day cycle, up to 8 cycles</li> </ul> <p>Diluted in a <b>500 mL</b> infusion bag of 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP</p> <p>Resulting in a final concentration between <b>0.2 mg/mL – 0.7 mg/mL</b></p> <p>Dose modifications are toxicity Grade specific.</p>	<ul style="list-style-type: none"> <li>NHL: 120 mg/m<sup>2</sup> infused intravenously over <b>10 minutes</b> on days 1 and 2 of a 21-day cycle, up to 8 cycles</li> </ul> <p>Diluted in a <b>50 mL</b> infusion bag of 0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, or <b>5% Dextrose Injection, USP</b></p> <p>Resulting in a final concentration between <b>1.85 mg/mL – 5.6 mg/mL</b></p> <p>Dose modifications are toxicity Grade specific.</p>
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We have evaluated the risks associated with this naming strategy and do not object to the use of a dual proprietary name in this case.

### **2.2.9 Communication of DMEPA’s Analysis at Midpoint of Review**

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on March 19, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DHP on March 21, 2018, they stated no additional concerns with the proposed proprietary name, Belrapzo.

## **3 CONCLUSION**

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Neil Vora, OSE project manager, at 240-402-4845.

### **3.1 COMMENTS TO THE APPLICANT**

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

If any of the proposed product characteristics as stated in your submission, received on February 2, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.



## 4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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

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

### *Drugs@FDA*

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

### *RxNorm*

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

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

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

### *Division of Medication Errors Prevention and Analysis proprietary name consultation requests*

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

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

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

## APPENDICES

### Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
  - a. **Preliminary Assessment:** We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2\*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>e</sup>

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<sup>e</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
<b>Y/N</b>	<b>Is the proposed name obviously similar in spelling and pronunciation to other names?</b>
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
<b>Y/N</b>	<b>Are there inert or inactive ingredients referenced in the proprietary name?</b>
	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)).
<b>Y/N</b>	<b>Does the proprietary name include combinations of active ingredients?</b>
	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)).
<b>Y/N</b>	<b>Is there a United States Adopted Name (USAN) stem in the proprietary name?</b>
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
<b>Y/N</b>	<b>Is this proprietary name used for another product that does not share at least one common active ingredient?</b>
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
<b>Y/N</b>	<b>Is this a proprietary name of a discontinued product?</b>
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score  $\geq 70\%$ .
  - Moderately similar pair: combined match percentage score  $\geq 55\%$  to  $\leq 69\%$ .
  - Low similarity: combined match percentage score  $\leq 54\%$ .

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  $\geq 70$  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<sup>f</sup>. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
  - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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<sup>f</sup> Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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

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

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

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

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

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

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

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

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

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

**Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is  $\geq 55\%$  to  $\leq 69\%$ ).**

<p>Step 1</p>	<p>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.</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>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.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.</li> <li>• Similar sounding doses: 15 mg is similar in sound to 50 mg</li> </ul>
<p>Step 2</p>	<p>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 <b>with</b> overlapping or similar strengths or doses.</p>

	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names?</li> <li>• Is there different number or placement of cross-stroke or dotted letters present in the names?</li> <li>• Do the infixes of the name appear dissimilar when scripted?</li> <li>• Do the suffixes of the names appear dissimilar when scripted?</li> </ul>	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• Do the names have different number of syllables?</li> <li>• Do the names have different syllabic stresses?</li> <li>• Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?</li> <li>• Across a range of dialects, are the names consistently pronounced differently?</li> </ul>
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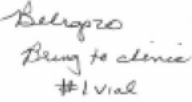
**Table 5: Low Similarity Name Pair Checklist (i.e., combined score is  $\leq 54\%$ ).**

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. Belrapzo Study (Conducted on 2/21/2018)**

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Belrapzo Bring to clinic #1 vial
<u>Outpatient Prescription:</u> 	

**FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)**

306 People Received Study

92 People Responded

Study Name: Belrapzo

Total	30	30	32	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
BEBRAPZS	0	0	1	1
BELARAPSO	0	1	0	1
BELARAPZO	1	0	0	1
BELIAPZO	0	0	1	1
BELRAPOZO	1	0	0	1
BELRAPRO	9	0	0	9
BELRAPSO	0	14	0	14
BELRAPYS	0	0	8	8
BELRAPYS CIDI	0	0	1	1
BELRAPZA	0	0	1	1
BELRAPZO	16	0	4	20

BELRAPZO OR BELRAPSO	0	1	0	1
BELRAPZS	0	0	15	15
BELRAPZYS	0	0	1	1
BELREMZO	0	1	0	1
BELROPZO	1	0	0	1
BELROYZO	1	0	0	1
BELSAPZO	1	0	0	1
BELWRAPSO	0	1	0	1
BLERAPSO	0	1	0	1
DALRAPSO	0	1	0	1
DARAZOL	0	1	0	1
ELRAPSO	0	2	0	2
L-RAPSO	0	1	0	1
OLRAPZO	0	1	0	1
VALRAPSO	0	3	0	3
VELRAPSO	0	1	0	1
VELRAPZO	0	1	0	1

**Appendix C:** Highly Similar Names (e.g., combined POCA score is  $\geq 70\%$ )

No.	Proposed name: Belrapzo Established name: Bendamustine HCl Dosage form: Injection Strength(s): 25 mg/mL Usual Dose: <ul style="list-style-type: none"> <li>• CLL: 100 mg/m<sup>2</sup> infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles</li> <li>• NHL: 120 mg/m<sup>2</sup> infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles</li> </ul> The dosing interval is one day of a 21 or 28-day cycle for up to 6 or 8 cycles. (b) (4)	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion  Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Belrapzo	100	Subject of this review.

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

No.	Name	POCA Score (%)
1.	Belsomra	63
2.	Benzepro	63
3.	(b) (4)***	56
4.	Bellatal	56
5.	Ferraplus	56
6.	Rabeprazole	54
7.	Omeprazole	50
8.	Brexpirozole	46

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

No.	<b>Proposed name: Belrapzo</b> <b>Established name: Bendamustine HCl</b> <b>Dosage form: Injection</b> <b>Strength(s): 25 mg/mL</b> <b>Usual Dose:</b> <ul style="list-style-type: none"> <li>• <b>CLL:</b> 100 mg/m<sup>2</sup> infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles</li> <li>• <b>NHL:</b> 120 mg/m<sup>2</sup> infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles</li> </ul> <b>The dosing interval is one day of a 21 or 28-day cycle for up to 6 or 8 cycles. The maximum daily dose is 280 mg/m<sup>2</sup>.</b>	<b>POCA Score (%)</b>	<b>Prevention of Failure Mode</b>  <b>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</b>
1.	Terazol 3	60	This name pair has sufficient orthographic and phonetic differences.
2.	Terazol 7	60	This name pair has sufficient orthographic and phonetic differences.
3.	Zaltrap	58	This name pair has sufficient orthographic and phonetic differences.
4.	Zelapar	58	<p>Orthographically, the first letters (B vs. Z) and suffixes (zo vs. ar) provide some differences. Phonetically, the second syllables (“-rap” vs. “-a-”) and third syllables (“-zo” vs. “-par”) provide sufficient phonetic difference for this name pair.</p> <p>Differences in product characteristics:  <u>Dosage form:</u> injection vs. orally disintegrating tablet  <u>Usual Dose and Frequency:</u> CLL: 100 mg/m<sup>2</sup> infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles or NHL: 120 mg/m<sup>2</sup> infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles vs. 1.25 mg to 2.5 mg daily  <u>Routes of Administration:</u> intravenous vs. oral</p>
5.	(b) (4) ***	54	This name pair has sufficient orthographic and phonetic differences.

No.	<b>Proposed name: Belrapzo</b> <b>Established name: Bendamustine HCl</b> <b>Dosage form: Injection</b> <b>Strength(s): 25 mg/mL</b> <b>Usual Dose:</b> <ul style="list-style-type: none"> <li>• <b>CLL:</b> 100 mg/m<sup>2</sup> infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles</li> <li>• <b>NHL:</b> 120 mg/m<sup>2</sup> infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles</li> </ul> <b>The dosing interval is one day of a 21 or 28-day cycle for up to 6 or 8 cycles. The maximum daily dose is 280 mg/m<sup>2</sup>.</b>	POCA Score (%)	<b>Prevention of Failure Mode</b>  <b>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</b>
6.	Darazol	40	<p>This name pair has sufficient orthographic and phonetic differences. Phonetically the first syllables (“Bel-” vs. “Dan”) of this name pair provide some phonetic differences. Orthographically, the prefixes (Bel vs. Dan), infixes (rap vs. a), and the presence of an upstroke letter “l” in the suffix of Danazol provide sufficient differences.</p> <p>Differences in Product Characteristics:  <u>Dosage form:</u> injection vs. capsule  <u>Route of Administration:</u> intravenous vs. oral  <u>Frequency:</u> once every 21- or 28-day cycle, for a total 6 to 8 cycles vs. 2 to 3 times daily</p>

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

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

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

No.	Name	POCA Score (%)	Failure preventions
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No.	Name	POCA Score (%)	Failure preventions
1.	Bedranol	60	International product marketed in the United Kingdom.
2.	Bellaspas	60	Product discontinued per Redbook; no generic equivalents available.
3.	Bellergal	59	Product discontinued per Redbook; no generic equivalents available.
4.	Bellamor	58	Product discontinued per Redbook; no generic equivalents available.
5.	Bel-Tabs	58	Product discontinued per Redbook; no generic equivalents available.
6.	Berocca Pn	58	Brand discontinued with no generic equivalent available. NDA 006071 withdrawn FR effective 04/26/1996.
7.	Bovapro	58	Veterinary Product.
8.	Telazol	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases
9.	Baratol	56	International product formerly marketed in South Africa, United Kingdom and Ireland.
10.	Bellaphen-S	55	Product discontinued per Redbook; no generic equivalents available.
11.	Bet-R-Prep	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases

**Appendix H:** Names not likely to be confused due to absence of attributes that are known to cause name confusion<sup>g</sup>.

No.	Name	POCA Score (%)
1.	Zelboraf	58
2.	(b) (4) ***	58
3.	Valrox	58
4.	Ertaczo	57
5.	Dermazor	56
6.	Zaleplon	56

<sup>g</sup> 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

No.	Name	POCA Score (%)
7.	(b) (4)***	56
8.	Zilretta	56
9.	Xeljanz	55

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/s/  
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