

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**213931Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

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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)  
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>	June 2, 2023
<b>Application Type and Number:</b>	NDA 213931
<b>Product Name and Strength:</b>	Xphozah (tenapanor hydrochloride) Tablets, 10 mg, 20 mg and 30 mg
<b>Product Type:</b>	Single Ingredient Product
<b>Rx or OTC:</b>	Prescription (Rx)
<b>Applicant/Sponsor Name:</b>	Ardelyx, Inc. (Ardelyx)
<b>PNR ID #:</b>	2023-1044725102
<b>DMEPA 2 Safety Evaluator:</b>	Christina Topper, PharmD, BCPS
<b>DMEPA 2 Team Leader:</b>	Hina Mehta, PharmD
<b>DMEPA 2 Director:</b>	Danielle Harris, PharmD

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## 1 INTRODUCTION

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

### 1.1 REGULATORY HISTORY

Ardelyx previously submitted the proposed proprietary name, (b) (4) \*\*\* on May 5, 2017 under IND 120566. However, we found the name, (b) (4) \*\*\* unacceptable due to similarity in spelling and orthographic similarities (b) (4) under IND 120566 on October 27, 2017.<sup>a</sup>

The Sponsor submitted the name, (b) (4) \*\*\*, for review on February 22, 2018 under IND 120566 which was found conditionally acceptable on August 14, 2018.<sup>b</sup> However, on January 20, 2023 the Sponsor submitted the proposed proprietary name, (b) (4) \*\*\* under IND 120566 and withdrew (b) (4) \*\*\* on January 30, 2020.

We found the name, (b) (4) \*\*\* unacceptable due to orthographic similarities and overlapping product characteristics with the currently marketed product Xpovio under IND 120566 and NDA 213931 on July 27, 2020.<sup>c</sup> Thus, Ardelyx submitted the name, Xphozah, for review on August 28, 2020 which was found conditionally acceptable on November 20, 2020.<sup>d</sup>

On July 28, 2021, a Complete Response Letter (CRL) was issued for NDA 213931. In response to the CRL, Ardelyx submitted a Class 2 Resubmission of the NDA and concurrently resubmitted the name Xphozah for review on April 17, 2023.

### 1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on April 17, 2023.

- Intended Pronunciation: ex foe' zah
- Active Ingredient: tenapanor hydrochloride
- Indication of Use: Control of serum phosphorous levels in patients with CKD on dialysis.

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<sup>a</sup> Lowery, A. Proprietary Name Review for (b) (4) (IND 120566). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 OCT 27. Panorama No. 2017-14880576.

<sup>b</sup> Straka, M. Proprietary Name Review for (b) (4) (IND 120566). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 AUG 14. Panorama No. 2018-21164890.

<sup>c</sup> Harris, D. Proprietary Name Review for (b) (4) (IND 120566 and NDA 213931). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 JUL 27. Panorama No. 2020-37545085 and 2020-40978381.

<sup>d</sup> Straka, M. Proprietary Name Review for Xphozah (NDA 213931). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 20. Panorama No. 2020-42444132.

- Route of Administration: Oral
- Dosage Form: Tablets
- Strength: 10 mg, 20 mg and 30 mg
- Dose and Frequency: 30 mg taken two times daily just prior to first and last meals of the day. The maximum daily dose is 60 mg/day.
- How Supplied:
  - Commercial: 10 mg, 20 mg and 30 mg
    - 60 count 60 mL round white HDPE bottle with the 33 mm CRC cap
    - 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap
  - Physician Samples: 10 mg, 20 mg and 30 mg
    - 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap
- Storage: Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Keep bottle tightly closed to protect from moisture. Store and dispense in original bottle with the desiccant.

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Xphozah 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 Xphozah. The Division of Cardiology and Nephrology (DCN) concurred with the findings of OPDP's assessment for Xphozah.

### 2.2 SAFETY ASSESSMENT

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

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

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

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

Ardelyx did not provide a derivation or intended meaning for the proposed proprietary name, Xphozah, in their submission. This proprietary name is comprised of a single word that does not

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<sup>e</sup> USAN stem search conducted on May 22, 2023.

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 May 15, 2023, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Xphozah at the initial phase of the review.

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

Ninety (N=90) practitioners participated in DMEPA’s prescription studies for Xphozah. 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<sup>f</sup> identified four (4) names with the combined score of  $\geq 55\%$  or individual orthographic or phonetic score of  $\geq 70\%$ . 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 one (1) name not previously analyzed. This name is 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.

<b>Table 1. Names Retrieved for Review Organized by Name Pair Similarity</b>	
<b>Similarity Category</b>	<b>Number of Names</b>
Highly similar name pair: combined match percentage score $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	1
Low similarity name pair: combined match percentage score $\leq 54\%$	0

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<sup>f</sup> POCA search conducted on May 22, 2023 in version 5.2.

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

Our analysis of the one (1) name contained in Table 1 determined none of the names will pose a risk for confusion with Xphozah as described in Appendices C through H.

### 2.2.8 Discussion of Dual Proprietary Names

Tenapanor is currently approved under the proprietary name, Ibsrela, under NDA 211801 for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults. Ardelyx intends to market tenapanor under the proprietary name, Xphozah, under NDA 213931. Table 2 compares the proposed proprietary name, Xphozah, with the currently approved Ibsrela and their respective product characteristics.

In the proprietary name submission from August 28, 2020, Ardelyx stated their failure modes and effects analysis (FMEA) determined that marketing the products under dual proprietary names would be “essentially equivalent from a risk perspective” as marketing the products under a single proprietary name.

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

**TABLE 2: COMPARISON OF XPHOZAH\*\*\* AND IBSRELA**

<b>Product</b>	<b>Xphozah*** (proposed) NDA 213931</b>	<b>Ibsrela NDA 211801</b>
<b>Active Ingredient</b>	Tenapanor	
<b>Indication of Use</b>	Control of serum phosphorus levels in adult patients with Chronic Kidney Disease on dialysis who have had an inadequate response or intolerance to a phosphate binder therapy.	Treatment of irritable bowel syndrome with constipation (IBS-C) in adults
<b>Route of Administration</b>	Oral	
<b>Dosage Form</b>	Tablets	
<b>Strength</b>	10 mg, 20 mg and 30 mg	50 mg
<b>Dose and Frequency</b>	Usual dosage: 30 mg by mouth twice daily; 60 mg/day max dose.	Usual dosage: 1 tablet by mouth twice daily (100 mg/day)
<b>How Supplied</b>	Commercial: 10 mg, 20 mg and 30 mg <ul style="list-style-type: none"> <li>60 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> </ul>	IBSRELA is supplied in a white, opaque, high-density polyethylene bottle containing 60 tablets with a silica gel canister (as the desiccant) and screw-top polypropylene child-resistant cap lined

	<ul style="list-style-type: none"> <li>14 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> </ul> Physician samples: 10 mg, 20 mg and 30 mg <ul style="list-style-type: none"> <li>14 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> </ul>	and induction- activated aluminum foil liner.
<b>Storage</b>	Store at room temperature, between 68°F and 77°F (20°C and 25°C).	

**2.2.9 Communication of DMEPA’s Determination**

On June 2, 2023, DMEPA 2 communicated our determination to the Division of Cardiology and Nephrology (DCN).

**3 CONCLUSION**

The proposed proprietary name, Xphozah, is conditionally acceptable.

If you have any questions or need clarifications, please contact Monique Killen, OSE project manager, at 240-402-1985.

## 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](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. <sup>g</sup>

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<sup>g</sup> 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.
<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, 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  $\geq 70\%$ .
  - 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>h</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>h</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.

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  $\geq 70\%$ ).**

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.

<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 z and f), 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  $\leq 69\%$ ).**

Step 1	<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>
Step 2	<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>

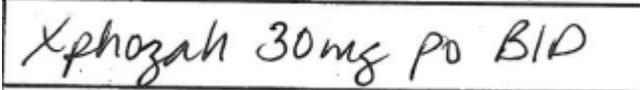
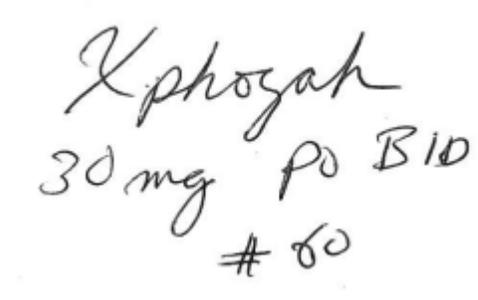
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</li> <li>• Are the lengths of the 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 ≤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. Xphozah Study (Conducted on April 28, 2023)**

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order:</p> 	<p>Xphozah</p> <p>Take 30 mg by mouth twice daily</p>
<p>Outpatient Prescription:</p> 	<p>Dispense 60</p>
<p><b>CPOE Study Sample (displayed as sans-serif, 12-point, bold font)</b></p>	
<p><b>Xphozah</b></p>	

**FDA Prescription Simulation Responses (Aggregate Report)**

Study Name: Xphozah

256 People Received Study  
90 People Responded

Total	25	23	20	22	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
EXFOSA	0	0	3	0	3
EXFOZA	0	0	9	0	9
EXPOSA	0	0	5	0	5
XFOSA	0	0	1	0	1
XFOSSA	0	0	1	0	1
XPHAZAH	1	0	0	0	1
XPHOGAH	0	0	0	8	8
XPHORZAH	0	0	0	1	1
XPHOYAH	0	0	0	1	1

XPHOZAH	23	23	0	11	57
XPOSA	0	0	1	0	1
XYPHOZA	1	0	0	0	1
ZPHOYAH	0	0	0	1	1

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

**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 -N/A

**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

<b>No.</b>	<b>Proposed name:</b> Xphozah <b>Established name:</b> tenapanor hydrochloride <b>Dosage form:</b> Tablets <b>Strength(s):</b> 10 mg, 20 mg and 30 mg <b>Usual Dose:</b> 30 mg taken two times daily just prior to first and last meals of the day.	<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.	Veozah***	65	<p>Orthographically, the names start with different first letters (X vs. V). Additionally, Xphozah contains the downstroke letter ‘p’ and upstroke letter ‘h’ at the beginning of the name, which is absent from Veozah***. These differences give the names different shapes when scripted.</p> <p>Phonetically, the first syllables (‘Ex’ vs. ‘Vee’) and the onset of the second syllables (‘foe’ vs. ‘oh’) sound different when spoken.</p> <p>Additionally, there is no direct overlap in strength (10 mg, 20 mg, and 30 mg vs. 45 mg) or frequency of administration (twice daily vs. once daily). Xphozah is also proposed to be available in multiple strengths, therefore a strength must be provided on a prescription order which provides additional differentiation.</p>

**Appendix F:** Low Similarity Names (e.g., combined POCA score is  $\leq 54\%$ ) – N/A

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

reasons described. – N/A

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

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<sup>i</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

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**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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/s/  
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CHRISTINA A TOPPER  
06/02/2023 12:08:04 PM

HINA S MEHTA  
06/02/2023 01:37:20 PM

DANIELLE M HARRIS  
06/02/2023 01:43:20 PM

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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>	November 20, 2020
<b>Application Type and Number:</b>	NDA 213931
<b>Product Name and Strength:</b>	Xphozah (tenapanor) Tablets, 10 mg, 20 mg and 30 mg
<b>Product Type:</b>	Single Ingredient Product
<b>Rx or OTC:</b>	Prescription (Rx)
<b>Applicant/Sponsor Name:</b>	Ardelyx, Inc. (Ardelyx)
<b>Panorama #:</b>	2020-42444132
<b>DMEPA Safety Evaluator:</b>	Maximilian Straka, PharmD, FISMP
<b>DMEPA Team Leader:</b>	Hina Mehta, PharmD

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## 1 INTRODUCTION

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

### 1.1 REGULATORY HISTORY

The Sponsor previously submitted the proposed proprietary name, (b) (4)\*\*\* on May 5, 2017. However, we found the name, (b) (4)\*\*\* unacceptable due to similarity in spelling and orthographic similarities (b) (4) under IND 120566 on October 27, 2017.<sup>a</sup>

The Sponsor submitted the name, (b) (4)\*\*\*, for review on February 22, 2018 which was found conditionally acceptable on August 14, 2018.<sup>b</sup>

However, the Sponsor prefers to market with the proposed proprietary name, (b) (4), instead of (b) (4)\*\*\* and submitted the proposed proprietary name, (b) (4), for review on January 30, 2020. Subsequently, the Sponsor withdrew (b) (4)\*\*\* on February 10, 2020.

We found the name, (b) (4)\*\*\* unacceptable due to orthographic similarities and overlapping product characteristics with the currently marketed product Xpovio under IND 120566 and NDA 213931 on July 27, 2020.<sup>c</sup> Thus, Ardelyx submitted the name, Xphozah, for review on August 28, 2020.

### 1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 28, 2020.

- Intended Pronunciation: ex foe' zah
- Active Ingredient: tenapanor
- Indication of Use: Control of serum phosphorus levels in patients with CKD on dialysis.
- Route of Administration: Oral
- Dosage Form: Tablets
- Strength: 10 mg, 20 mg and 30 mg

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<sup>a</sup> Lowery, A. Proprietary Name Review for (b) (4) (IND 120566). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Oct 27. Panorama No. 2017-14880576.

<sup>b</sup> Straka, M. Proprietary Name Review for (b) (4) (IND 120566). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 Aug 14. Panorama No. 2018-21164890.

<sup>c</sup> Harris, D. Proprietary Name Review for (b) (4) (IND 120566 and NDA 213931). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Jul 27. Panorama No. 2020-37545085 and 2020-40978381.

- Dose and Frequency: 30 mg taken two times daily. The maximum daily dose is 60 mg/day.
- How Supplied:
  - Commercial: 10 mg, 20 mg and 30 mg
    - 60 count 60 mL round white HDPE bottle with the 33 mm CRC cap
    - 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap
  - Physician Samples: 10 mg, 20 mg and 30 mg
    - 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap
- Storage: Store at room temperature, between 68°F and 77°F (20°C and 25°C). Keep in original container and protect from moisture. Keep the container tightly closed and in a dry place. Do not remove desiccant from the bottle. Do not subdivide or repackage.

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Xphozah would not misbrand the proposed product, however they “would like to note the phonetic and orthographic similarities to the approved and marketed tradename, Xofluza.” We address this name pair in Appendix F below. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Cardiology and Nephrology (DCN) concurred with the findings of OPDP’s assessment for Xphozah.

### 2.2 SAFETY ASSESSMENT

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

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

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

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

Ardelyx did not provide a derivation or intended meaning for the proposed proprietary name, Xphozah, 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.

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<sup>d</sup> USAN stem search conducted on October 16, 2020.

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

In response to the OSE, September 30, 2020 e-mail, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Xphozah at the initial phase of the review.

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

Eighty-six (86) practitioners participated in DMEPA's prescription studies for Xphozah. 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<sup>e</sup> identified 3 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 and other disciplines. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

<b>Table 1. Names Retrieved for Review Organized by Name Pair Similarity</b>	
<b>Similarity Category</b>	<b>Number of Names</b>
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	1
Low similarity name pair: combined match percentage score $\leq 54\%$	1

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

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

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<sup>e</sup> POCA search conducted on October 16, 2020 in version 4.4.

### 2.2.8 Discussion of Dual Proprietary Names

Tenapanor is currently approved under the proprietary name, Ibsrela, under NDA 211801 for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults. Ardelyx intends to market tenapanor under the proprietary name: Xphozah (NDA 213931). Table 2 compares the proposed proprietary name Xphozah with the currently approved Ibsrela and their respective product characteristics.

In the August 28, 2020, proprietary name submission, Ardelyx stated their failure modes and effects analysis (FMEA) determined that marketing the products under dual proprietary names would be essentially equivalent from a risk perspective as marketing the products under a single proprietary name.

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

**Table 2: Comparison of Xphozah\*\*\* and Ibsrela**

<b>Product</b>	<b>Xphozah*** (proposed) NDA 213931</b>	<b>Ibsrela NDA 211801</b>
<b>Active Ingredient</b>	Tenapanor	
<b>Indication of Use</b>	Control of serum phosphorus levels in patients with CKD on dialysis	Irritable Bowel Syndrome-Constipation (IBS-C)
<b>Route of Administration</b>	Oral	
<b>Dosage Form</b>	Tablets	
<b>Strength</b>	10 mg, 20 mg and 30 mg	50 mg
<b>Dose and Frequency</b>	Usual dosage: 30 mg by mouth twice daily; 60 mg/day max dose.	Usual dosage: 1 tablet by mouth twice daily (100 mg/day)
<b>How Supplied</b>	Commercial: 10 mg, 20 mg and 30 mg <ul style="list-style-type: none"> <li>• 60 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> <li>• 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> </ul> Physician samples: 10 mg, 20 mg and 30 mg <ul style="list-style-type: none"> <li>• 14 count 60 mL round white HDPE bottle with the 33 mm CRC cap</li> </ul>	IBSRELA is supplied in a white, opaque, high-density polyethylene bottle containing 60 tablets with a silica gel canister (as the desiccant) and screw-top polypropylene child-resistant cap lined and induction-activated aluminum foil liner.
<b>Storage</b>	Store at room temperature, between 68°F and 77°F (20°C and 25°C).	

### 2.2.9 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiology and Nephrology (DCN) via e-mail on November 16, 2020. At that time we also requested additional information or

concerns that could inform our review. Per e-mail correspondence from the Division of Cardiology and Nephrology (DCN) on November 16, 2020, they stated no additional concerns with the proposed proprietary name, Xphozah.

### **3 CONCLUSION**

The proposed proprietary name, Xphozah, is acceptable.

If you have any questions or need clarifications, please contact Wana Manitpisitkul, OSE project manager, at 240-402-4156.

#### **3.1 COMMENTS TO ARDELYX, INC.**

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

If any of the proposed product characteristics as stated in your submission, received on August 28, 2020, 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](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.<sup>f</sup>

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<sup>f</sup> 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.
<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>§</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

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<sup>§</sup> 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. 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  $\geq 70\%$ ).**

<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 render the names less likely to confusion, provided that the pair does not share a common strength or dose.</p>			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
<b>Y/N</b>	<p>Do the names begin with different first letters?</p> <p><i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i></p>	<b>Y/N</b>	<p>Do the names have different number of syllables?</p>
<b>Y/N</b>	<p>Are the lengths of the names dissimilar* when scripted?</p> <p><i>*FDA considers the length of names different if the names differ by two or more letters.</i></p>	<b>Y/N</b>	<p>Do the names have different syllabic stresses?</p>
<b>Y/N</b>	<p>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?</p>	<b>Y/N</b>	<p>Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?</p>
<b>Y/N</b>	<p>Is there different number or placement of cross-stroke or dotted letters present in the names?</p>	<b>Y/N</b>	<p>Across a range of dialects, are the names consistently pronounced differently?</p>
<b>Y/N</b>	<p>Do the infixes of the name appear dissimilar when scripted?</p>		
<b>Y/N</b>	<p>Do the suffixes of the names appear dissimilar when scripted?</p>		

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

Step 1	<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>
Step 2	<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>

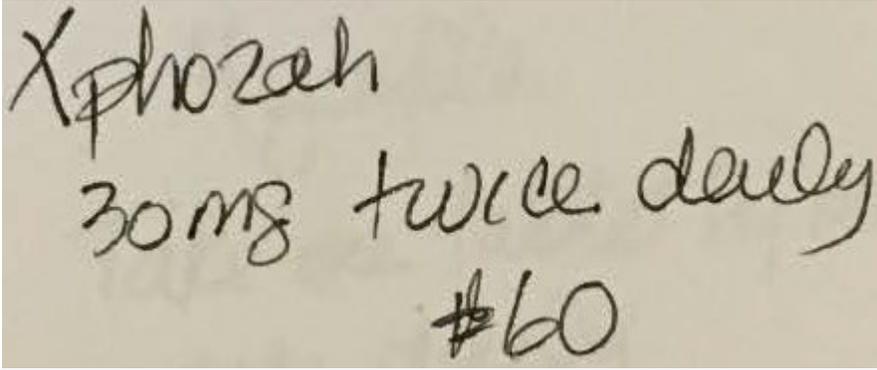
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</li> <li>• Are the lengths of the 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 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 ≤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. Xphozah Study (Conducted on October 23, 2020)**

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order:</p> <p>Xphozah 30mg po bid</p>	<p>Xphozah 30 mg twice daily # 60</p>
<p>Outpatient Prescription:</p> 	
<p><b>CPOE Study Sample (displayed as sans-serif, 12-point, bold font)</b></p>	
<p>Xphozah</p>	

**FDA Prescription Simulation Responses (Aggregate Report)**

**Study Name: Xphozah**

As of Date 11/6/2020

210 People Received Study

86 People Responded

Study Name: Xphozah

	<b>Total</b>	<b>17</b>	<b>32</b>	<b>20</b>	<b>17</b>	
<b>INTERPRETATION</b>	<b>OUTPATIENT</b>	<b>CPOE</b>	<b>VOICE</b>	<b>INPATIENT</b>	<b>TOTAL</b>	
EXFOPA	0	0	1	0	1	
EXFOSA	0	0	2	0	2	
EXFOZA	0	0	9	0	9	
EXPHOSA	0	0	1	0	1	
EXPHOZA	0	0	1	0	1	
EXPOSA	0	0	5	0	5	
EXVOZA	0	0	1	0	1	
KPHOZAH	0	0	0	1	1	
XPHOZA	1	0	0	0	1	
XPHOZAH	16	32	0	15	63	
XPHZAH	0	0	0	1	1	

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

No.	Proposed name: Xphozah Established name: tenapanor Dosage form: Tablets Strength(s): 10 mg, 20 mg and 30 mg Usual Dose: 30 mg by mouth twice daily.	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion  Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Xphozah***	100	This name is the subject of this review.
2.	(b) (4)***	85	Proposed proprietary name for IND 120566 and NDA 213931 found unacceptable by DMEPA (OSE# 2020-37545085 and 2020-40978281). NDA 213931 currently under review with proposed proprietary name Xphozah*** which is the 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.	Dvorah	62

**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.	Proposed name: Xphozah Established name: tenapanor Dosage form: Tablets Strength(s): 10 mg, 20 mg and 30 mg Usual Dose: 30 mg by mouth twice daily.	POCA Score (%)	Prevention of Failure Mode  In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	N/A		

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

No.	Name	POCA Score (%)
1.	Xofluza	54

**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.	N/A		

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

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

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<sup>h</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

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/s/

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MAXIMILIAN STRAKA  
11/20/2020 11:49:46 AM

HINA S MEHTA  
11/20/2020 12:52:56 PM

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## Proprietary Name Review Memorandum

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>	July 27, 2020
<b>Application Type and Number:</b>	IND 120566 and NDA 213931
<b>Product Name and Strength:</b>	(b) (4) (tenapanor) tablets 10 mg, 20 mg, 30 mg
<b>Product Type:</b>	Single Ingredient Product
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Ardelyx
<b>Panorama #:</b>	2020-37545085 and 2020-40978381
<b>DMEPA Deputy Director:</b>	Danielle Harris, PharmD

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/s/  
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07/27/2020 04:09:48 PM

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