

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204441Orig1s000**

**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>	January 23, 2018
<b>Application Type and Number:</b>	NDA 204441
<b>Product Name and Strength:</b>	Jynarque (Tolvaptan) tablets, 15 mg, 30 mg, 45 mg, 60 mg, 90 mg
<b>Product Type:</b>	Single-Ingredient Product
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Otsuka America Pharmaceutical, Inc.
<b>Panorama #:</b>	2017-18604395
<b>DMEPA Safety Evaluator:</b>	Sarah Thomas, PharmD
<b>DMEPA Team Leader:</b>	Chi-Ming (Alice) Tu, PharmD, BCPS

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## 1 INTRODUCTION

This review evaluates the proposed proprietary name, Jynarque, 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 the (b) (4) for this product.

### 1.1 REGULATORY HISTORY

Since 2009, Otsuka has been marketing Tolvaptan tablets in the United States under the proprietary name, Samsca, for the treatment of clinically significant hypervolemic and euvolemic hyponatremia.

In 2012, Otsuka submitted a 505(b)(1) New Drug Application (NDA 204441) for tolvaptan for the treatment of autosomal dominant polycystic kidney disease (ADPKD).

Prior to NDA submission at a July 2012 pre-NDA meeting, the Food and Drug Administration (FDA) agreed that a new proprietary name was appropriate for the newly proposed ADPKD indication.

On January 25, 2013, Otsuka submitted a request for the review of the proposed dual proprietary name, (b) (4)\*\*\*, under NDA 204441. DMEPA held a teleconference with Otsuka on March 25, 2013 to discuss safety concerns with the proposed dual trade name, specifically the Agency did not have enough safety information on tolvaptan-induced hepatotoxicity to assess the appropriateness of allowing a dual proprietary name for tolvaptan. Therefore, we recommended Otsuka withdraw the proposed proprietary name, (b) (4)\*\*\*. The proposed proprietary name was withdrawn on April 4, 2013 from NDA 204441.

On July 15, 2013, the proposed proprietary name, (b) (4)\*\*\*, was subsequently submitted for review under NDA 204441, and then withdrawn again on September 20, 2013 after NDA 204441 received a complete response on August 28, 2013.

On March 15, 2017, the proposed proprietary name, (b) (4)\*\*\*, was submitted for review under IND 72975, with an amendment submitted on May 10, 2017 containing the risk assessment for use of a dual proprietary name. (b) (4)

On (b) (4), we found the name, (b) (4)\*\*\* unacceptable due to phonetic similarities and shared product characteristics with the proprietary name, (b) (4).<sup>a</sup>

Thus, the Applicant submitted the name, Jynarque, for review on October 27, 2017 under NDA 204441.

### 1.2 PRODUCT INFORMATION

The following product information is provided in the October 27, 2017 proprietary name submission.

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<sup>a</sup>Thomas, S. Proprietary Name Review for (b) (4)\*\*\* (b) (4) Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); (b) (4). Panorama No. (b) (4).

- Intended Pronunciation: jin ar kew
- Active Ingredient: Tolvaptan
- Indication of Use: Selective vasopressin V2-receptor antagonist that slows kidney function decline [REDACTED] (b) (4) in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD)
- Route of Administration: Oral
- Dosage Form: Tablets
- Strengths: 15 mg, 30 mg, 45 mg, 60 mg, 90 mg
- Dose and Frequency: The initial dose is 60 mg orally daily as a split-dose regimen (45 mg taken on waking and 15 mg taken 8 hours later). The initial dose should be titrated upward to a split-dose regimen of 90 mg per day (60 mg taken on waking and 30 mg taken 8 hours later), and then to a target 120 mg per day (90 mg taken on waking and 30 mg taken 8 hours later) if tolerated with at least weekly intervals between titrations. Patients may be down-titrated to lower doses based on tolerability and should be maintained on the highest tolerable dose.
- How Supplied: Cartons containing 4 [REDACTED] (b) (4), each containing a 7-day dosage regimen blister card of 14 tablets: combination of 15 mg and 45 mg strengths, combination of 30 mg and 60 mg strengths, or combination of 30 mg and 90 mg (7 tablets of each strength per blister card); distributed via a REMS program
- Storage: Store at 25 °C (77 °F), excursions permitted between 15 °C and 30 °C (59 °F to 86 °F) [see USP controlled Room Temperature].

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

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

### 2.2 SAFETY ASSESSMENT

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

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

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

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<sup>b</sup> USAN stem search conducted on November 6, 2017.

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

The Applicant did not provide a derivation or intended meaning for the proposed name, Jynarque, 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, November 9, 2017 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

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

Ninety-three practitioners participated in DMEPA's prescription studies, with 59 practitioners in the outpatient and inpatient studies interpreting Jynarque correctly. 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. Of note, 1 participant in the study reported that Jynarque (b) (4)

[REDACTED] Otsuka has submitted new proposed proprietary name Jynarque under NDA, the subject of this review. [REDACTED] <sup>(b) (4)</sup>\*\*\* is further evaluated in Appendix G. 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>c</sup> identified 17 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 with Strength Overlap and Potential Orthographic, Spelling, and Phonetic Similarities**

The proposed product, Jynarque, will be available in 15 mg, 30 mg, 45 mg, 60 mg, and 90 mg strength(s). Since the 90 mg strength is not a typical strength that is commonly marketed, we searched the Electronic Drug Registration and Listing System (eDRLS) database to identify names with strength overlap. Names with strength overlap and potential orthographic, spelling, and phonetic similarities with Jynarque that were not identified in POCA include Jadenu and Ginseng Khan. These names are included in Table 1 below. Other names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences are listed in Appendix I.

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<sup>c</sup> POCA search conducted on November 6, 2017 in version 4.2. POCA tool updated to incorporate a revised orthographic algorithm.

**2.2.7 Names Retrieved for Review Organized by Name Pair Similarity**

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

<b>Table 1. 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 $\leq 69\%$	17
Low similarity name pair: combined match percentage score $\leq 54\%$	6

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

Our analysis of the 23 names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

**2.2.9 Evaluation of Dual Proprietary Names**

We previously evaluated the use of dual proprietary names for Samsca and the proposed product in OSE Review #2017-13758406 dated September 6, 2017 under IND 072975, and concluded that we do not object to the use of dual proprietary names.<sup>a</sup> Upon reassessment, we note there's been no change in product characteristics for Samsca or the proposed product since our last review. We maintain our position and do not object to the use of a dual proprietary naming strategy in this case.

**2.2.10 Communication of DMEPA's Analysis at Midpoint of Review**

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on January 19, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on January 22, 2018, they stated no additional concerns with the proposed proprietary name, Jynarque.

**3 CONCLUSIONS**

The proposed proprietary name is acceptable.

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

**3.1 COMMENTS TO THE APPLICANT**

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

If any of the proposed product characteristics as stated in your October 27, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

## REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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

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

### ***Drugs@FDA***

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

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<sup>d</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>e</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.,

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

route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

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

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

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

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

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

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

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

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

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

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 vowel reduction, assimilation, or deletion?

Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

**Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is  $\geq 55\%$  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>
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Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <b>with</b> overlapping or similar strengths or doses.	
	<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>

**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. Jynarque Study (Conducted on November 9, 2017)**

Handwritten Medication Order/Prescription	Verbal Prescription												
<p>Medication Order:</p> <table border="1"> <tr> <td>DATE</td> <td>TIME</td> <td>Jynarque 60mg/30mg 60mg tablet</td> <td></td> </tr> <tr> <td>DATE</td> <td>TIME</td> <td>upon waking, then 30mg tablet</td> <td></td> </tr> <tr> <td>DATE</td> <td>TIME</td> <td>8 hours later</td> <td></td> </tr> </table>	DATE	TIME	Jynarque 60mg/30mg 60mg tablet		DATE	TIME	upon waking, then 30mg tablet		DATE	TIME	8 hours later		<p>Jynarque 45 mg/15 mg</p> <p>Take one 45 mg tablet upon waking, and then take one 15 mg tablet 8 hours later</p> <p>Dispense 1 Carton</p>
DATE	TIME	Jynarque 60mg/30mg 60mg tablet											
DATE	TIME	upon waking, then 30mg tablet											
DATE	TIME	8 hours later											
<p>Outpatient Prescription:</p> <div style="border: 1px solid black; padding: 10px;"> <p>Patient _____ Date <u>11/9/17</u></p> <p>Address _____</p> <p><b>R</b></p> <p>Jynarque 45mg/15mg</p> <p>Take one 45 mg tab upon waking, and then one 15 mg tab 8 hours later.</p> <p>Dispense 1 carton</p> <p>  </p> <p>Refill(s): _____ Dr. <u>Ose</u></p> <p>DEA No. _____ Address _____</p> <p>Telephone _____</p> </div>													

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

**Study Name: Jynarque**

As of Date 11/27/2017

297 People Received Study

93 People Responded

Study Name: Jynarque

<b>Total</b>	<b>29</b>	<b>28</b>	<b>36</b>	
<b>INTERPRETATION</b>	<b>OUTPATIENT</b>	<b>VOICE</b>	<b>INPATIENT</b>	<b>TOTAL</b>
GENAQUE	0	1	0	1
GENARCUE	0	5	0	5
GENARQ	0	4	0	4
GENAR-Q	0	1	0	1
GENARQU	0	1	0	1
GENARQUE	0	10	0	10
GENOCUE	0	1	0	1
GINARQUE	0	2	0	2
JANARQ	0	1	0	1
JENARCU	0	1	0	1
JENARQUE	0	1	0	1
JYMARQUE	0	0	1	1
JYNARQUE	27	0	32	59
JYNARYUE	0	0	2	2
TYNARQUE	2	0	1	3

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

No.	<b>Proposed name:</b> Jynarque <b>Established name:</b> Tolvaptan <b>Dosage form:</b> Tablets <b>Strength(s):</b> 15 mg, 30 mg, 45 mg, 60 mg, 90 mg <b>Usual Dose:</b> Initial dose is 60 mg orally daily as a split-dose regimen (45 mg taken on waking and 15 mg taken 8 hours later), and titrated up to 90 mg per day (60 mg taken on waking and 30 mg taken 8 hours later) and then to a target 120 mg per day (90 mg taken on waking and 30 mg taken 8 hours later)	<b>POCA Score (%)</b>	<b>Orthographic and/or phonetic differences in the names sufficient to prevent confusion</b>  <b>Other prevention of failure mode expected to minimize the risk of confusion between these two names.</b>
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

No.	Name	POCA Score (%)
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

No.	<b>Proposed name:</b> Jynarque <b>Established name:</b> Tolvaptan <b>Dosage form:</b> Tablets <b>Strength(s):</b> 15 mg, 30 mg, 45 mg, 60 mg, 90 mg <b>Usual Dose:</b> Initial dose is 60 mg orally daily as a split-dose regimen (45 mg taken on waking and 15 mg taken 8 hours later), and titrated up to 90 mg per day (60 mg taken on waking and 30 mg taken 8 hours later) and then to a target 120 mg per day (90 mg taken on waking and 30 mg taken 8 hours later)	<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.	Dynacirc	55	This name pair has sufficient orthographic and phonetic differences.
2.	Dynafreeze	56	This name pair has sufficient orthographic and phonetic differences.
3.	Garlique	56	This name pair has sufficient orthographic and phonetic differences.
4.	Gelnique	59	This name pair has sufficient orthographic and phonetic differences.
5.	Ginseng Khan	32	This name pair has sufficient orthographic and phonetic differences.
6.	Jadenu	46	This name pair has sufficient orthographic and phonetic differences.
7.	Synarel	58	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
8.	(b) (4)	43
9.	Januvia	46
10.	Jinteli	42
11.	Narcan	48

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

No.	Name	POCA Score (%)	Failure preventions
12.	Gelnique 3 %	59	"Gelnique 3 %" identified in AIMS record as associated with NDA 202513, which per Drugs@FDA is discontinued with no TE codes provided and per DARRTS has a status of "Withdrawn FR Effective."
13.	Gelnique 3%	59	Brand discontinued with no generic equivalents available per Drugs@FDA, Clinical Pharmacology, Facts and Comparisons, and Micromedex Redbook databases.
14.	Hypaque	56	Brand discontinued with no TE Code provided per Drugs@FDA database. Hypaque sodium 100% powder off the market per Clinical Pharmacology database, and Hypaque M is discontinued with no generic equivalents available per Micromedex Redbook database. Hypaque formerly marketed per tox and drug product lookup database.
15.	Hypaque 76	56	Brand discontinued with no generic equivalents available per Drugs@FDA and Micromedex Redbook databases.
16.	Hypaque-76	56	Brand discontinued with no generic equivalents available per Drugs@FDA and Micromedex Redbook databases.
17.	(b) (4)***	64	Proposed proprietary name by Otsuka found unacceptable by DMEPA on (b) (4) 7 under IND 072975 (Panorama #: (b) (4)). Otsuka has submitted new proposed proprietary name Jynarque under NDA, the subject of this review.
18.	(b) (4)***	62	Proposed proprietary name found acceptable by DMEPA on (b) (4) (b) (4) under NDA (b) (4) NDA (b) (4) is withdrawn per DARRTS.
19.	Ryna Liquid	60	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
20.	Tenar Pse	60	Brand discontinued with no generic equivalents available per Micromedex Redbook database.
21.	Dynacirc Cr	56	Brand discontinued with no generic equivalents available per Drugs@FDA, Clinical Pharmacology, and Micromedex Redbook databases.

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

No.	Name	POCA Score (%)
22.	Ben-Aqua	64
23.	Synjardy	59

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

No.	Name
1.	Adalat CC
2.	Adenosine
3.	Albuterol
4.	albuterol sulfate
5.	Antara
6.	Armour Thyroid
7.	ASIAN GINSENG
8.	AVINZA
9.	Benzocaine hydrochloride
10.	BRILINTA
11.	Budesonide
12.	Cardizem
13.	Cheong-Kwan-Jang      Korean HongSam
14.	cinacalcet hydrochloride
15.	Crinone
16.	daclatasvir
17.	DAKLINZA
18.	deferasirox
19.	Diltiazem Hydrochloride
20.	fenofibrate
21.	Fluoxetine hydrochloride
22.	Isopropyl Alcohol
23.	lanreotide acetate
24.	metoprolol succinate
25.	minocycline hydrochloride
26.	Morphine sulfate
27.	NeutraCaine
28.	Nifediac CC

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<sup>f</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
29.	nifedipine
30.	Nitrogen
31.	PANAX GINSENG FRUIT
32.	PROAIR
33.	ProAir RespiClick
34.	PROAIRHFA
35.	Procardia
36.	Prochieve
37.	progesterone
38.	Prozac
39.	PULMICORT
40.	rolapitant
41.	Sensipar
42.	Somatuline Depot
43.	STELARA
44.	THYROID, PORCINE
45.	Ticagrelor
46.	Umbiliclean
47.	ustekinumab
48.	Varubi
49.	VENTOLIN
50.	Ximino

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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01/23/2018

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01/23/2018