# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 215559Orig1s000

# PROPRIETARY NAME REVIEW(S)

**PROPRIETARY NAME MEMORANDUM**

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

| | |
|---|---|
| **Date of This Review:** | April 14, 2023 |
| **Application Type and Number:** | NDA 215559 |
| **Product Name and Strength:** | Sohonos (palovarotene) capsule, 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | Prescription (Rx) |
| **Applicant/Sponsor Name:** | Ipsen Biopharmaceuticals, Inc. (Ipsen) |
| **PNR ID #:** | 2023-1044725002 |
| **DMEPA 1 Safety Evaluator:** | Corwin D. Howard, PharmD |
| **DMEPA 1 Acting Team Leader:** | Madhuri R. Patel, PharmD |
| **DMEPA 1 Director:** | Mishale Mistry, PharmD, MPH |

# 1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Sohonos, which was found conditionally acceptable under NDA 215559 on August 8, 2022.[a] However, NDA 215559 received a Complete Response (CR) action on December 23, 2023 due to clinical deficiencies[b]. Thus, Ipsen submitted the name, Sohonos, under NDA 215559 for review on February 16, 2023 as part of the resubmission to the CR. We note that all product characteristics remain the same.

# 2 METHODS AND DISCUSSION

## 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Sohonos would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Sohonos. The Division of General Endocrinology (DGE) concurred with the findings of OPDP's assessment for Sohonos.

## 2.2 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, we 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 proposed proprietary name. Our reassessment did not change our conclusion regarding the previously identified names of concern. Additionally, we searched the United States Adopted Name (USAN) stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The April 9, 2023 search of USAN stems did not find any USAN stems in the proposed proprietary name, Sohonos.

## 2.3 COMMUNICATION OF DMEPA'S DETERMINATION

On April 14, 2023, we communicated our determination to the Division of General Endocrinology (DGE).

# 3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Sohonos, is conditionally acceptable.

If you have any questions or need clarifications, please contact Deveonne Hamilton-Stokes, OSE project manager, at 301-796-2253.

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[a] Howard, C. Proprietary Name Review for Sohonos (NDA 215559). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 AUG 08. PNR ID No. 2022-1044724587.

[b] Yanoff, L. Communication: Complete Response Letter for palovarotene capsules (NDA 215559). Silver Spring (MD): FDA, CDER, OND, DGE (US); 2022 DEC 23. Available from: https://darrts fda.gov/darrts/faces/ViewDocument?documentId=090140af806a542a

### 3.1 COMMENTS TO IPSEN BIOPHARMACEUTICALS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on February 16, 2023, are altered prior to approval of the marketing application, the name must be resubmitted for review.

REFERENCE

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

   USAN Stems List contains all the recognized USAN stems.

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/s/

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CORWIN D HOWARD
04/14/2023 08:15:24 PM

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**PROPRIETARY NAME REVIEW**

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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| | |
|---|---|
| **Date of This Review:** | August 8, 2022 |
| **Application Type and Number:** | NDA 215559 |
| **Product Name and Strength:** | Sohonos (palovarotene) capsule, 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | Prescription (Rx) |
| **Applicant/Sponsor Name:** | Ipsen Biopharmaceuticals, Inc. (Ipsen) |
| **PNR ID #:** | 2022-1044724587 |
| **DMEPA 1 Safety Evaluator:** | Corwin D. Howard, PharmD, RPh |
| **Acting DMEPA 1 Team Leader:** | Madhuri R. Patel, PharmD |
| **DMEPA 1 Associate Director for Nomenclature and Labeling:** | Mishale Mistry, PharmD, MPH |

Contents

# 1 INTRODUCTION

This review evaluates the proposed proprietary name, Sohonos, 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. Ipsen submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

## 1.1 REGULATORY HISTORY

Ipsen previously submitted the proposed proprietary name, (b) (4) *** on February 5, 2018. However, we found the name, (b) (4) *** unacceptable due to orthographic similarities and shared product characteristics with 1) the proprietary name, (b) (4) and 2) pending proprietary name, (b) (4) *** under IND 120181 on May 3, 2018.[a] Thus, Clementia submitted the name, Sohonos, for review on January 23, 2019. We found the name Sohonos*** conditionally acceptable under IND 120181 on April 23, 2019.[b]

Subsequently, Ipsen (Clementia was acquired by Ipsen) submitted the name, Sohonos***, for review on March 31, 2021 under NDA 215559 and we found the name Sohonos*** conditionally acceptable on June 7, 2021.[c] However, NDA 215559 was withdrawn on August 12, 2021.

Thus, Ipsen resubmitted NDA 215559 on April 29, 2022 and submitted the name, Sohonos, for review on May 13, 2022.

## 1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on May 13, 2022.

- Intended Pronunciation: soh-HO-nos
- Active Ingredient: palovarotene
- Indication of Use: prevention of heterotopic ossification (HO) in adults and children (aged 8 years and above for females and 10 years and above for males) with fibrodysplasia ossificans progressiva (FOP).
- Route of Administration: oral
- Dosage Form: capsule
- Strength: 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg

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[a] Karpow, C. Proprietary Name Review for (b) (4) *** (IND 120181). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 MAY 03. Panorama No. 2018-20817156.

[b] Karpow, C. Proprietary Name Review for Sohonos*** (IND 120181). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Apr 23. Panorama No. 2019-28813944.

[c] Holmes, L. Proprietary Name Review for Sohonos**** (NDA 215559). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 JUN 07. Panorama No. 2021-1044723900.

- Dose and Frequency:

  Chronic/Flare-Up Regimen:

  The recommended dosing regimen is 5 mg once daily (chronic regimen) with an increase in dose at the time of flare-up to 20 mg once daily for 4 weeks followed by 10 mg once daily for 8 weeks for a total of 12 weeks (20/10 mg flare-up treatment regimen), even if symptoms resolve earlier.

  Flare-up treatment should begin at the onset of the first symptom indicative of a FOP flare-up or substantial high-risk traumatic event likely to lead to a flare-up. Symptoms of a FOP flare-up typically include but are not limited to localized pain, soft tissue swelling/inflammation, redness, warmth, decreased joint range of motion, and stiffness. Chronic treatment should cease at the time of initiation of flare-up treatment; re-initiation of the 5 mg daily treatment should occur after completion of the flare-up treatment. Weight-adjusted dosage is required in children who are under 14 years of age (see Table 1).

  Flare-ups can occur in the absence of any apparent causative factor, but there is a high risk that substantial traumatic events (e.g: surgery, intramuscular immunization, mandibular blocks for dental work, muscle fatigue, blunt muscle trauma from bumps, bruises, falls, or influenza-like viral illnesses), can lead to a flare-up and result in heterotopic bone formation. Flare-up treatment should be initiated at the time of such events.

  In the presence of persistent flare-up symptoms, treatment may be extended in 4-week intervals with 10 mg SOHONOS and continued until the flare-up symptoms resolve.

  Should the patient experience another flare-up (new flare-up location or marked worsening of the original flare-up) at any time during flare-up treatment, the flare-up 12-week treatment should be restarted.

  Dose adjustment in children under 14 years of age:

  Sohonos dosing is weight-adjusted in patients under 14 years of age (see Table 1). The physician should prescribe the most appropriate dosage based on weight for children aged from 8 years (females) and 10 years (males) to less than 14 years.

**Table 1: Weight-Adjusted Dosage for Children < 14 Years**

| | Chronic Dosing | Flare up (Weeks 1 to 4) | Flare up (Weeks 5 to 12) |
|---|---|---|---|
| ≥60kg* | 5 mg | 20 mg | 10 mg |
| 40-<60kg | 4 mg | 15 mg | 7.5 mg |
| 20-<40kg | 3 mg | 12.5 mg | 6 mg |
| 10-<20kg | 2.5 mg | 10 mg | 5 mg |

*All children ≥14 years of age and adults will receive the dose in the ≥60 kg weight category.

If a dose of medication is missed, patients should take a missed dose as soon as possible. If the dose has been missed by more than 6 hours, instruct the patient to skip the missed dose and continue with the next scheduled dose. Instruct the patient to not take two doses at the same time or in the same day.

Dosage Modification for Adverse Reactions:

If the patient experiences intolerable adverse effects during SOHONOS treatment, the daily dose should be reduced to the next lower dosage as shown in Table 2; additional dose reduction should occur if adverse reactions continue to be intolerable. If the patient is already receiving the lowest possible dose, then consideration should be given to discontinue therapy temporarily or permanently (b) (4) Subsequent flare-up treatment should be initiated at the same reduced treatment that was tolerated previously.

**Table 2: Dose Reduction of SOHONOS**

| Dose Prescribed | Reduced Dose |
|---|---|
| 20 mg | 15 mg |
| 15 mg | 12.5 mg |
| 12.5 mg | 10 mg |
| 10 mg | 7.5 mg |
| 7.5 mg | 5 mg |
| 6 mg | 4 mg |
| 5 mg | 2.5 mg |
| 4 mg | 2 mg |
| 3 mg | 1.5 mg |
| 2.5 mg | 1 mg |

(b) (4)

- How Supplied: 1 mg, 1.5 mg, 5.5 mg, 5 mg, and 10 mg - Packaged as one 14 capsules blister strip with aluminum foil lidding encased in a cardboard card inserted in a child resistant carton.

- Storage: [redacted] (b) (4) Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room temperature]. PROTECT FROM LIGHT.

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Sohonos would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Sohonos. The Division of General Endocrinology (DGE) did not comment on the findings of OPDP's assessment for Sohonos.

### 2.2 SAFETY ASSESSMENT

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

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

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

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

Ipsen did not provide a derivation or intended meaning for the proposed proprietary name, Sohonos, in their submission. This proprietary name is comprised of a single word that contains the ending letters "-os" which is the abbreviation for "left eye". This abbreviation was evaluated in our previous review, and we agree with our previous findings.[e] Beyond this abbreviation, we note that Sohonos does not contain any components (i.e., a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

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

On June 2, 2022, the Division of General Endocrinology (DGE) did not forward any comments or concerns relating to Sohonos at the initial phase of the review.

#### *2.2.4 FDA Name Simulation Studies*

One hundred and two (n=102) practitioners participated in DMEPA's prescription studies for Sohonos. The responses did not overlap with any currently marketed products nor did the

[d] USAN stem search conducted on June 3, 2022.

[e] Holmes, L. Proprietary Name Review for Sohonos**** (NDA 215559). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 JUN 07. Panorama No. 2021-1044723900.

responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

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

Our POCA search[f] identified 18 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed, and we agree with the findings from our previous review for the names evaluated previously. Therefore, we did not identify any new names.

### *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 (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

**Table 1. Names Retrieved for Review Organized by Name Pair Similarity**

| Similarity Category | Number of Names |
|---|---|
| Highly similar name pair:<br>combined match percentage score ≥70% | 2 |
| Moderately similar name pair:<br>combined match percentage score ≥55% to ≤ 69% | 0 |
| Low similarity name pair:<br>combined match percentage score ≤54% | 0 |

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

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

### *2.2.8 Communication of DMEPA's Determination*

On August 8, 2022, DMEPA 1 communicated our determination to the Division of General Endocrinology (DGE).

## 3 CONCLUSION

The proposed proprietary name, Sohonos, is acceptable.

[f] POCA search conducted on June 10, 2022 in version 4.4.

If you have any questions or need clarifications, please contact Deveonne Hamilton-Stokes, OSE project manager, at 301-796-2253.

### 3.1 COMMENTS TO IPSEN BIOPHARMACEUTICALS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on May 13, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

## 4 REFERENCES


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

USAN Stems List contains all the recognized USAN stems.

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

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

***Drugs@FDA***

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

***RxNorm***

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

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

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

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

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

## APPENDICES

### Appendix A

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

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

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

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

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

| | Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance. |
|---|---|
| **Y/N** | **Is the proposed name obviously similar in spelling and pronunciation to other names?** |
| | Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products. |
| **Y/N** | **Are there inert or inactive ingredients referenced in the proprietary name?** |
| | Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)). |
| **Y/N** | **Does the proprietary name include combinations of active ingredients?** |
| | Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)). |
| **Y/N** | **Is there a United States Adopted Name (USAN) stem in the proprietary name?** |
| | Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem. |
| **Y/N** | **Is this proprietary name used for another product that does not share at least one common active ingredient?** |
| | Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name. |
| **Y/N** | **Is this a proprietary name of a discontinued product?** |
| | Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients. |

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

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[h]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

| | |
|---|---|
| Step 1 | Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation.<br><br>For single strength products, also consider circumstances where the strength may not be expressed.<br><br>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.<br><br>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:<br><br>• 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.<br><br>• Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.<br><br>• Similar sounding doses: 15 mg is similar in sound to 50 mg |
| Step 2 | Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses. |

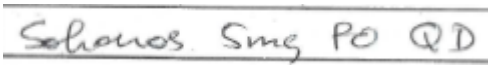
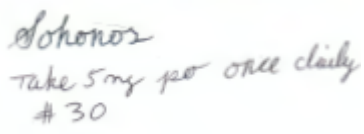
| | | |
|---|---|---|
| | Orthographic Checklist (Y/N to each question)<br>• Do the names begin with different first letters?<br>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.<br>• Are the lengths of the names dissimilar* when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

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

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

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

**Figure 1. Sohonos Study (Conducted on June 10, 2022)**

| **Handwritten Medication Order/Prescription** | | **Verbal Prescription** |
|---|---|---|
| Medication Order: |  | Sohonos<br>Take 5 mg by mouth once daily.<br>Dispense #30 |
| Outpatient Prescription: |  | |
| **CPOE Study Sample (displayed as sans-serif, 12-point, bold font)** | | |
| **Sohonos** | | |

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

Study Name: Sohonos

262 People Received Study
102 People Responded

| Total | 21 | 31 | 21 | 29 | |
|---|---|---|---|---|---|
| INTERPRETATION | INPATIENT | CPOE | VOICE | OUTPATIENT | TOTAL |
| SAHONAS | 0 | 0 | 4 | 0 | 4 |
| SAHONES | 0 | 0 | 2 | 0 | 2 |
| SAHONESS | 0 | 0 | 2 | 0 | 2 |
| SAHONIS | 0 | 0 | 6 | 0 | 6 |
| SAHONYS | 0 | 0 | 1 | 0 | 1 |
| SAHOONUS | 0 | 0 | 1 | 0 | 1 |
| SEHONAS | 0 | 0 | 1 | 0 | 1 |
| SEHONIS | 0 | 0 | 1 | 0 | 1 |
| SOHANOS | 1 | 0 | 0 | 0 | 1 |
| SOHONAS | 0 | 0 | 2 | 0 | 2 |
| SOHONOA | 0 | 0 | 0 | 1 | 1 |
| SOHONOG | 0 | 0 | 0 | 1 | 1 |
| SOHONOR | 0 | 0 | 0 | 14 | 14 |
| SOHONOS | 16 | 31 | 0 | 10 | 57 |
| SOHONOZ | 0 | 0 | 0 | 3 | 3 |
| SOHOUOS | 1 | 0 | 0 | 0 | 1 |
| SOLIANOS | 1 | 0 | 0 | 0 | 1 |
| SOLINOS | 1 | 0 | 0 | 0 | 1 |
| SOLROUOS | 1 | 0 | 0 | 0 | 1 |
| SUHONESS | 0 | 0 | 1 | 0 | 1 |

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

| No. | **Proposed name:** Sohonos<br>**Established name:** palovarotene<br>**Dosage form:** capsule<br>**Strength(s):** 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg<br>**Usual Dose:** 1 capsule once daily | **POCA Score (%)** | **Orthographic and/or phonetic differences in the names sufficient to prevent confusion**<br><br>**Other prevention of failure mode expected to minimize the risk of confusion between these two names.** |
|---|---|---|---|
| 1. | Sohonos | 100 | Subject of this review. |
| 2. | Hongos | 71 | Orthographically, the first letters (S' vs. 'H'') are different. Additionally, Sohonos has the upstroke letter 'h' in the infix position, where Hongos has a downstroke letter 'g' in the infix position.<br><br>Phonetically, the word pair differs in syllables. Sohonos has 3 syllables (soh-HO-nos) vs Hongos 2 syllables (Hon-gos). The first syllable (soh) provides sufficient phonetic differences.<br><br>In addition to orthographic and phonetic differences, the following product characteristics may help to minimize the risk of error:<br>• Sohonos is available in multiple strengths (*1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg*) and the strength needs to be included on a prescription or medication order for Sohonos.<br>• The products vary in frequency of administration (*twice daily vs. once daily*).<br>• No overlap in route of administration (*topical vs. oral*) and dosage form (*topical cream vs. capsule*), which if included on the medication order/prescription, may help to differentiate between the products.<br><br>When all the aforementioned mitigations are considered in totality, we find the risk of confusion is adequately minimized in this case. |

**Appendix D:** Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose: **– N/A**

**Appendix E:** Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose: **– N/A**

**Appendix F:** Low Similarity Names (e.g., combined POCA score is ≤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[i].: **– N/A**

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

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**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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CORWIN D HOWARD
08/08/2022 11:11:24 AM

MADHURI R PATEL
08/08/2022 11:13:54 AM

MISHALE P MISTRY
08/08/2022 11:25:42 AM

**PROPRIETARY NAME REVIEW**

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

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

| | |
|---|---|
| **Date of This Review:** | June 7, 2021 |
| **Application Type and Number:** | NDA 215559 |
| **Product Name and Strengths:** | Sohonos (palovarotene) capsule, 1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | Prescription (Rx) |
| **Applicant/Sponsor Name:** | Ipsen Biopharmaceuticals, Inc. (Ipsen) |
| **PNR ID #:** | 2021-1044723900 |
| **DMEPA Safety Evaluator:** | Loretta Holmes, BSN, PharmD |
| **DMEPA Team Leader:** | Sevan Kolejian, PharmD, MBA, BCPPS |
| **DMEPA Director:** | Lubna Merchant, MS, PharmD |

Contents

# 1 INTRODUCTION

This review evaluates the proposed proprietary name, Sohonos, 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. Ipsen submitted an external name study, conducted by [redacted], for this proposed proprietary name.

## 1.1 REGULATORY HISTORY

Clementia previously submitted the proposed proprietary name, [redacted]*** on February 5, 2018. However, we found the name, [redacted]*** unacceptable due to orthographic similarities and shared product characteristics with the proprietary name, [redacted] and pending proprietary name, [redacted]*** under IND 120181 on May 3, 2018.[a] Thus, Clementia submitted the name, Sohonos, for review on January 23, 2019. We found the name Sohonos conditionally acceptable under IND 120181 on April 23, 2019.[b]

Subsequently, Ipsen (Clementia was acquired by Ipsen) submitted the name, Sohonos, for review under NDA 215559 on March 31, 2021. Product Information

## 1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on March 31, 2021.

- Intended Pronunciation: soh-HO-nos
- Active Ingredient: palovarotene
- Indication of Use: the prevention of heterotopic ossification in adults and children (aged 8 years and above for females and 10 years and above for males) with fibrodysplasia (myositis) ossificans progressiva (FOP)
- Route of Administration: Oral
- Dosage Form: Capsule
- Strengths: 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg
- Dose and Frequency:

  Chronic/Flare-Up Regimen

  The recommended dosing consists of 5 mg once daily (chronic treatment), with an increase in dose at the time of a flare-up to 20 mg once daily for 4 weeks, followed by 10 mg once daily for 8 weeks for a total of 12 weeks (20/10 mg flare-up treatment), even if symptoms resolve earlier.

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[a] Karpow, C. Proprietary Name Review for [redacted] (IND 120181). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 MAY 03. Panorama No. 2018-20817156.

[b] Karpow, C. Proprietary Name Review for Sohonos (IND 120181). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Apr 23. Panorama No. 2019-28813944.

Flare-up treatment should begin at the onset of the first symptom indicative of a FOP flare-up or substantial high-risk traumatic event likely to lead to a flare-up. Symptoms of a FOP flare-up typically include but are not limited to localized pain, soft tissue swelling/inflammation, redness, warmth, decreased joint range of motion, and stiffness. Chronic treatment should cease at the time of initiation of flare-up treatment; re-initiation of the 5 mg daily treatment should occur after completion of the flare-up treatment. Weight-adjusted dosage is required in children who are under 14 years of age (see Table 1).

Flare-ups can occur in the absence of any apparent causative factor, but there is a high risk that substantial traumatic events (e.g., surgery, intramuscular immunization, mandibular blocks for dental work, muscle fatigue, blunt muscle trauma from bumps, bruises, falls, or influenza-like viral illnesses), can lead to a flare-up and result in heterotopic bone formation. Flare-up treatment should be initiated at the time of such events.

In the presence of persistent flare-up symptoms, treatment may be extended in 4-week intervals with 10 mg Sohonos and continued until the flare-up symptoms resolve.

Should the patient experience another flare-up (new flare-up location or marked worsening of the original flare-up) at any time during flare-up treatment, the flare-up 12-week treatment should be restarted.

Dose adjustment in children under 14 years of age

Sohonos dosing is weight-adjusted in patients under 14 years of age (see Table 1). The physician should prescribe the most appropriate dosage based on weight for children aged from 8 years (females) and 10 years (males) to less than 14 years

**Table 1: Weight-Adjusted Dosage for Children < 14 Years**

| | Chronic Dosing | Flare up (Weeks 1 to 4) | Flare up (Weeks 5 to 12) |
|---|---|---|---|
| **≥60kg*** | 5 mg | 20 mg | 10 mg |
| **40-<60kg** | 4 mg | 15 mg | 7.5 mg |
| **20-<40kg** | 3 mg | 12.5 mg | 6 mg |
| **10-<20kg** | 2.5 mg | 10 mg | 5 mg |

*All children ≥14 years of age and adults will receive the dose in the ≥60 kg weight category.

Dosage Modification for Adverse Reactions

If the patient experiences intolerable adverse effects during SOHONOS treatment, the daily dose should be reduced to the next lower dosage as shown in Table 2; additional dose reduction should occur if adverse reactions continue to be intolerable. If the patient is already receiving the lowest possible dose, then consideration should be given to discontinue therapy temporarily or permanently (b) (4)

(b) (4) Subsequent flare-up treatment should be initiated at the same reduced treatment that was tolerated previously.

**Table 2: Dose Reduction of SOHONOS**

| Dose Prescribed | Reduced Dose |
|---|---|
| 20 mg | 15 mg |
| 15 mg | 12.5 mg |
| 12.5 mg | 10 mg |
| 10 mg | 7.5 mg |
| 7.5 mg | 5 mg |
| 6 mg | 4 mg |
| 5 mg | 2.5 mg |
| 4 mg | 2 mg |
| 3 mg | 1.5 mg |
| 2.5 mg | 1 mg |

- How Supplied: 1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg
  Packaged as one 14 capsules blister strip with aluminum foil lidding encased in a cardboard card inserted in a child-resistant carton
- Storage: Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room temperature]. Protect from light.

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Sohonos would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of General Endocrinology (DGE) concurred with the findings of OPDP's assessment for Sohonos.

### 2.2 SAFETY ASSESSMENT

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

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

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

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

Ipsen indicated in their submission that the proposed proprietary name, Sohonos, is "derived from a combination of letters that is devoid of meaning." This proprietary name is comprised of

[c] USAN stem search conducted on May 7, 2021.

a single word that contains the ending letters "os" which is the abbreviation for "left eye" and is used in writing prescriptions. Thus, the proposed name Sohonos could be interpreted as "Sohon OS", with "OS" as the intended route of administration (left eye). A POCA search of the name "Sohon" did not identify any names that would pose a risk for confusion.[d] Furthermore, the letters "os" are not separated from the name, capitalized, or bolded to make the letters "os" more prominent in the name. We also note that Sohonos will be available in a capsule dosage form so it is unlikely that the inclusion of the abbreviation "os" in the name will result in wrong route of administration errors with this product. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that we do not object to the inclusion of the letters "os" in this case. Beyond this abbreviation, we note that Sohonos does not contain any additional 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*

On April 15, 2021, the Division of General Endocrinology (DGE) did not forward any comments or concerns relating to Sohonos at the initial phase of the review.

### *2.2.4 FDA Name Simulation Studies*

Seventy-five (75) practitioners participated in DMEPA's prescription studies for Sohonos. The responses did 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. One participant in the inpatient study commented "could also be seen as Soronos" and one participant in the verbal study commented "sounds like 'soho' in NYC or theranos (fraudulent company)." However, these participants did not provide the name cited in their comment as a study response, nor did their comments indicate these were drug names of concern. Therefore, these names are unlikely to pose a risk for confusion. Appendix B contains the results from the prescription simulation studies.

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

Our POCA search[e] identified 18 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name.

We note that in our previous review[f], the following capsule strengths were proposed and considered ( (b) (4) capsules). However, the Applicant's proprietary name request under the NDA proposes the following strengths (1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg capsules). Although, the proposed strengths under the NDA

[d] POCA search conducted on May 13, 2021 in version 4.4.

[e] POCA search conducted on May 7, 2021 in version 4.4.

[f] Karpow, C. Proprietary Name Review for Sohonos (IND 120181). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Apr 23. Panorama No. 2019-28813944.

differ from the proposed strengths under the IND, the currently proposed strengths were evaluated in our previous review of Sohonos. Thus, the potential for numerical overlap or similarity of these strengths were previously reviewed and has been evaluated. We note that none of the other product characteristics have changed and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified one 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 new names retrieved from our POCA search and the (b) (4) external study that were not previously analyzed. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

**Table 1. Names Retrieved for Review Organized by Name Pair Similarity**

| Similarity Category | Number of Names |
|---|---|
| Highly similar name pair:<br>combined match percentage score ≥70% | 0 |
| Moderately similar name pair:<br>combined match percentage score ≥55% to ≤ 69% | 1 |
| Low similarity name pair:<br>combined match percentage score ≤54% | 5 |

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

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

### *2.2.8 Communication of DMEPA's Analysis at Midpoint of Review*

DMEPA communicated our findings to the Division of General Endocrinology (DGE). At that time, we also requested additional information or concerns that could inform our review. On June 3, 2021, the Division of General Endocrinology (DGE) stated no additional concerns with the proposed proprietary name, Sohonos.

## 3 CONCLUSION

The proposed proprietary name, Sohonos, is acceptable.

If you have any questions or need clarifications, please contact Phuong B. Nguyen, OSE Project Manager, at 240-402-5827.

### 3.1 COMMENTS TO IPSEN BIOPHARMACEUTICALS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on March 31, 2021, 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.

3. ***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).

4. ***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).

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

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

## APPENDICES

### Appendix A

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

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

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

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

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

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

| Y/N | Does the proprietary name include combinations of active ingredients? |
|---|---|
| | Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)). |
| **Y/N** | **Is there a United States Adopted Name (USAN) stem in the proprietary name?** |
| | Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem. |
| **Y/N** | **Is this proprietary name used for another product that does not share at least one common active ingredient?** |
| | Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name. |
| **Y/N** | **Is this a proprietary name of a discontinued product?** |
| | Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients. |

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.

- Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[h]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
- Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

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

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

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 ≥ 70%).**

| Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose. | | | |
|---|---|---|---|
| Orthographic Checklist | | Phonetic Checklist | |
| **Y/N** | Do the names begin with different first letters?<br>*Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.* | **Y/N** | Do the names have different number of syllables? |
| **Y/N** | Are the lengths of the names dissimilar* when scripted?<br>**FDA considers the length of names different if the names differ by two or more letters.* | **Y/N** | Do the names have different syllabic stresses? |
| **Y/N** | Considering variations in scripting of some letters (such as *z* and *f*), is there | **Y/N** | Do the syllables have different phonologic processes, such |

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

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

| | |
|---|---|
| Step 1 | Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation.<br><br>For single strength products, also consider circumstances where the strength may not be expressed.<br><br>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.<br><br>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:<br><br>• 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.<br><br>• Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. |

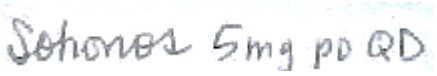
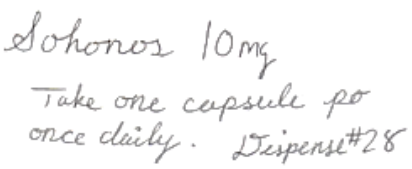
<table>
<tr><td></td><td colspan="2">• Similar sounding doses: 15 mg is similar in sound to 50 mg</td></tr>
<tr><td rowspan="2">Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</td></tr>
<tr><td>Orthographic Checklist (Y/N to each question)<br>• Do the names begin with different first letters?<br>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.<br>• Are the lengths of the names dissimilar* when scripted?<br>*FDA considers the length of names different if the names differ by two or more letters.<br>• 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?<br>• Is there different number or placement of cross-stroke or dotted letters present in the names?<br>• Do the infixes of the name appear dissimilar when scripted?<br>• Do the suffixes of the names appear dissimilar when scripted?</td><td>Phonetic Checklist (Y/N to each question)<br>• Do the names have different number of syllables?<br>• Do the names have different syllabic stresses?<br>• Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?<br>• Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

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

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

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

**Figure 1. Sohonos Study (Conducted on April 23, 2021)**

| Handwritten Medication Order/Prescription | Verbal Prescription |
|---|---|
| Medication Order:<br>  <br> | Sohonos 10 mg<br>Take one capsule by mouth once daily<br>Dispense #28 |
| Outpatient Prescription:<br>  <br> | |
| **CPOE Study Sample (displayed as sans-serif, 12-point, bold font)** | |
| Sohonos | |

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

| | | | | | |
|---|---|---|---|---|---|
| | | | | **205 People Received Study** | |
| | | | | **75 People Responded** | |
| **Study Name: Sohonos** | | | | | |
| **Total** | **15** | **27** | **15** | **18** | |
| **INTERPRETATION** | **OUTPATIENT** | **CPOE** | **VOICE** | **INPATIENT** | **TOTAL** |
| SOHONOS | 15 | 27 | 8 | 12 | 62 |
| SOHONOSE | 0 | 0 | 4 | 0 | 4 |
| SOHONOZ | 0 | 0 | 2 | 0 | 2 |
| SOTIONOS | 0 | 0 | 0 | 2 | 2 |
| SOTRONOS | 0 | 0 | 0 | 4 | 4 |
| ZOHONOS | 0 | 0 | 1 | 0 | 1 |

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

**Appendix D:** Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose – **N/A**

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

| **No.** | **Proposed name:**<br>Sohonos<br>**Established name:**<br>palovarotene<br>**Dosage form:**<br>Capsule<br>**Strengths:**<br>1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg<br>**Usual Dose:**<br>Dosage range: 1 mg to 20 mg orally once daily | **POCA Score (%)** | **Prevention of Failure Mode**<br><br>**In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names** |
|---|---|---|---|
| 1. | Seconal | 56 | This name pair has sufficient orthographic and phonetic differences. |

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

| **No.** | **Name** | **POCA Score (%)** |
|---|---|---|
| 1. | Sonata | 52 |
| 2. | Sotalol | 42 |
| 3. | Suboxone | 42 |
| 4. | Soma | 41 |
| 5. | Saphris | 38 |

**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[i]. – **N/A**

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

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/s/

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