

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

201656Orig1s000

PROPRIETARY NAME REVIEW(S)

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:	May 26, 2016
Application Type and Number:	NDA 201656
Product Name and Strength:	Noctiva (desmopressin nasal spray) 7.5 mcg/mL and 15 mcg/mL (0.75 mcg/0.1 mL and 1.5 mcg/0.1 mL)
Product Type:	Combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Serenity Pharmaceuticals, LLC
Panorama #:	2016-3056117
DMEPA Deputy Director:	Irene Z. Chan, PharmD, BCPS
DMEPA Director:	Todd Bridges, RPh

1. REASON FOR REVIEW

The memorandum is written because DMEPA management disagrees with some of CAPT Fava's position with respect to the acceptability of the proposed proprietary name, Noctiva, for desmopressin nasal spray (NDA 201656), and we describe the points of disagreement below. This memorandum is intended to summarize DMEPA's overall decision based on our evaluation of the draft review (Panorama # 2016-3056117), and the Proprietary Name Request submitted to NDA 201656 dated March 14, 2016.

2. MATERIALS REVIEWED

We reviewed the following materials:

- Review authored by CAPT Walter Fava (attached)
- Proposed proprietary name request for Noctiva dated March 14, 2016

3. DISCUSSION

CAPT Fava documents a concern that the name Noctiva is prone to confusion with another proposed name under review, Nocdurna***. He states that the orthographic similarity of Noctiva and Nocdurna*** coupled with the overlapping product characteristics may increase the risk for wrong drug errors. We agree based on his analysis and the POCA score that the names Noctiva and Nocdurna*** are orthographically similar. CAPT Fava points out that the FDA Phonetic and Orthographic Computer Analysis (POCA) combined score is 62% for the name pair, suggesting moderate similarity. However, despite sharing the identical prefix letters, 'Noc', and the same last letter 'a', we do identify some orthographic differences in the infixes of the names, 'tiv' vs. 'durn'. We believe the differences in the infixes of the name pair provide sufficient orthographic differentiation between the names. Specifically, Noctiva contains the cross stroke letter 't' in the 4th position that is not present in Nocdurna***, and the letter string 'tiv' also appears shorter than the letter string 'durn' when scripted. The differences are supported by the interpretations in our simulated studies where all participants included the letter "t" in their name interpretations. CAPT Fava indicates that these differences may not sufficiently differentiate this name pair and cites precedent with Neupogen (b) (4) confusion. However, we disagree and determined that these differences are difficult to overlook when the names are scripted. We note that the Neupogen (b) (4) cases involve products with similar dosage forms that may have contributed to the errors, which is not the case with Noctiva and Nocdurna*** (Noctiva is a nasal spray whereas Nocdurna*** is an orally disintegrating sublingual tablet).

CAPT Fava also asserts that Noctiva and Nocdurna*** share overlapping product characteristics that potentiate the risk for medication errors¹. He notes that both share the same active ingredient (desmopressin), same indication of use (adult nocturia), same frequency of administration (once nightly at bedtime) and have similar units of measure (mcg/mL vs. mcg). CAPT Fava acknowledges that despite these similarities, Noctiva has multiple strengths proposed in the NDA submission (7.5 mcg/mL and 15 mcg/mL) that differ from the strengths proposed for Nocdurna*** (25 mcg and 50 mcg) and that the products have two different routes of administration (nasal vs. sublingual), but asserts that the 7.5 mcg/mL strength may look similar to the 25 mcg strength when scripted and prescribers may omit the route of administration on orders for either product. However, we determined that the dose “1 spray” vs. “1 tablet” should also be considered and would be difficult to overlook on a prescription for these products.

Although CAPT Fava acknowledges that the products have different routes of administration, he cites precedent of confusion with Celebrex and Cerebyx, a drug name pair with a combined calculated POCA score of 71%, to illustrate that wrong drug errors can occur even in the absence of overlapping routes of administration when there is high orthographic similarity. We considered this information carefully, and we find the cited precedent case to be compelling to support the fact that wrong drug errors can occur even in the absence of overlapping routes of administration. Additionally, for highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as route of administration. However, we note that in this case of Noctiva vs. Nocdurna***, the combined POCA score calculated for this name pair is 62%, suggesting moderate similarity as opposed to high similarity. As noted above, we do identify some orthographic differences between the names.

CAPT Fava also expresses a concern that Noctiva and Nocdurna*** will appear immediately after one another on CPOE dropdown menus given the identical prefix letter string ‘Noc’. He cites precedent of confusion with Brilinta and Brintellix, which were confused despite not having overlapping strengths. We do not find this precedent case to be compelling as Brilinta and Brintellix are both oral solid dosage forms, whereas Noctiva is a nasal spray and Nocdurna*** is an orally disintegrating sublingual tablet. We find it unlikely that CPOE users would readily overlook the differences in the strength and route of administration during prescribing within an electronic system, where all of these elements are likely to be present during the order entry process. We also note that there are other approved proprietary names on the market that overlap in the first three letters with a risk for appearing next to or near one another on a drop down

¹ Noctiva (desmopressin) nasal spray is indicated for the treatment of adult nocturia with once daily dosing of a single spray in either the left or right nostril each night before bedtime. The applicant indicates the product will be available in a 7.5 mcg/mL and 15 mcg/mL strength, however, the statement of strength is still under review by OPQ. Nocdurna*** (desmopressin) orally disintegrating sublingual tablets are indicated for the treatment of adult nocturia with once daily dosing of 25 mcg for women and 50 mcg for men (b) (6). The applicant indicates the product will be available in a 25 mcg and 50 mcg strength.

menu, yet we have not identified a trend for name confusion error cases based on this point of similarity alone.

Furthermore, CAPT Fava asserts that confusion with Valtrex and Valcyte, which share a 3 letter string prefix in both the proprietary and established names, may be predictive of confusion with Noctiva and Nocdurna***, however, Valtrex and Valcyte share overlapping routes of administration, which again may have potentiated the risk for confusion with the name pair.

Finally, CAPT Fava states that given both names are pending and currently under review, it is possible that these products may be introduced to the market in close proximity to one another, which may result in practitioners having difficulty discerning the product characteristics. Thus, he concludes that, if approved, Noctiva may be confused with Nocdurna*** in the marketplace, resulting in situations of under dose and over dose in the event the wrong drug errors. However, given the orthographic differences in the names and differentiated product characteristics, we disagree.

In summary, although the proprietary names, Noctiva and Nocdurna***, are similar, we do not agree that the confusion would likely result in errors in the clinical setting. CAPT Fava identified no other safety or regulatory basis for recommending against the acceptance of the Noctiva name at this time. We reviewed the remainder of his evaluation and did not identify any outstanding concerns.

4. CONCLUSIONS AND RECOMMENDATIONS

We conclude that the proposed proprietary name, Noctiva, for desmopressin nasal spray (NDA 201656) is conditionally acceptable and recommend that this be conveyed to the applicant.

4.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your March 14, 2016 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

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)
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7.5 mcg/mL and 15 mcg/mL
(0.75 mcg/0.1 mL and 1.5 mcg/0.1 mL)
Product Type: Combination Product
Rx or OTC: Rx
Applicant/Sponsor Name: Serenity Pharmaceuticals, LLC
Panorama #: 2016-3056117
DMEPA Primary Reviewer: Walter Fava, RPh. MEd., Safety Evaluator
DMEPA Team Leader: Danielle Harris, PharmD., BCPS

Contents

1	INTRODUCTION.....	1
1.1	Regulatory History.....	1
1.2	Product Information.....	1
2	RESULTS.....	2
2.1	Misbranding Assessment.....	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS.....	4
3.1	Comments to the Applicant.....	4
4	REFERENCES.....	6
	APPENDICES.....	7

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Noctiva, under IND 76667 on June 5, 2014. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Noctiva, conditionally acceptable at that time in OSE Review #2014-25585, dated September 29, 2014.

Thus, the Applicant re-submitted the name, Noctiva, for re-review under NDA 201656 on March 14, 2016.

1.2 PRODUCT INFORMATION

The following product information is provided in the March 14, 2016 proprietary name submission.

- Intended Pronunciation: noc tiva
- Active Ingredient: desmopressin acetate
- Indication of Use: adult nocturia
- Route of Administration: Intranasal
- Dosage Form: Nasal Spray
- Strength:
 - The applicant submitted the strengths for this product as 7.5 mcg/mL and (b) (6) mcg/mL
 - Internal discussions regarding the statement of strength are ongoing. Based on information from CMC, (b) (4) respectively. Additionally, the CMC reviewer has stated that the statement of strength will likely be presented as XX mcg /0.1 mL to reflect the mcg strength per spray versus the mcg strength per mL. Therefore the strength presentations that have been considered for this review include:
 - Desmopressin 7.5 mcg/mL and 0.75 mcg/0.1 mL (per spray)
 - Desmopressin 15 mcg/mL and 1.5 mcg/0.1 mL (per spray)
 - Desmopressin acetate (b) (4) (per spray)
 - Desmopressin acetate (b) (4) (per spray)

- Dose and Frequency: Administered intra-nasally as a single spray in either the left or right nostril each night before bedtime. Patients should make every effort to administer the dose approximately 30 minutes prior to bedtime.
- How Supplied/Container Closure System: (b) (4) amber glass container that is fitted with a spray pump unit cap.
- Storage: Controlled Room Temperature 20 - 25°C (68 - (b) (4))

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. DMEPA and the Division of Bone, Reproductive, and Urologic Products (DBRUP) 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 name².

2.2.2 *Components of the Proposed Proprietary Name*

The Applicant did not provide a derivation or intended meaning for the proposed name, Noctiva 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 *FDA Name Simulation Studies*

Seventy-five practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

²USAN stem search conducted on April 4, 2016.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 23, 2016 e-mail, the Division of Bone, Reproductive, and Urologic Products (DBRUP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of $\geq 50\%$ retrieved from our POCA search³ organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	105
Low similarity name pair: combined match percentage score $\leq 49\%$	0

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

We determined 105 of the 106 of names will not pose a risk for confusion as described in Appendix C through H. However, the proposed name could be confused with Nocdurna^{***}. The rationale for the risk of confusion is described below.

The proposed proprietary name, Noctiva, is orthographically similar to the proposed name of another product that is also under review, Nocdurna^{***} (desmopressin orally disintegrating sublingual tablet, NDA 22517), and the products share overlapping product characteristics that may increase the risk of wrong drug errors.

The orthographic similarity between this name pair stems from their similar length (7 letters vs. 8 letters), shape (both names have an upstroke letter, ‘t’ vs. ‘d’ in similar positions), and both names begin with the identical first three letters, ‘Noc’. The names also both end with the letter, ‘a’, and the next to last letter of this name pair, (‘v’ vs. ‘n’) may look similar when scripted. The orthographic similarity is supported by the FDA Phonetic and Orthographic Computer Analysis (POCA), which calculates a combined score of 62% for the name pair, indicating moderate similarity. Although the names have some orthographic differences in the infixes (‘tiv’ vs. ‘durn’), we are concerned that these

³ POCA search conducted on March 25, 2016.

differences may be overlooked given the identical letter string at the beginning of the name. We have seen similar errors with other products that begin with identical letters and have some differences in the suffixes, for example, a pharmacist misread an order and dispensed Neupogen in place of [REDACTED]^{(b) (4)}.⁴ Additionally, Computer Provider Order Entry (CPOE) systems that auto-populate the name field or present a drop down menu after entry of the first three letters present a vulnerable point at which name confusion errors can occur. We are concerned that selection errors may occur by healthcare providers when utilizing CPOE systems, since it is likely these names will appear immediately after one another on drop down menus and they both contain the same active ingredient. Numerous medication errors involving name confusion with Brilinta and Brintellix, a name pair with an identical prefix letter string, have also been reported despite a POCA combined score of 50%. The continued reports led to a proprietary name change of Brintellix, whereby the first letter of the name was modified, changing the name to Trintellix. In a Drug Safety Communication (DSC) issued on July 30, 2015, FDA states that five of the errors for this name pair involved wrong product selection on CPOE order systems. In an article, Institute for Safe Medication Practices (ISMP) described an error in electronic prescribing in which a physician was attempting to prescribe Brintellix but incorrectly selected Brilinta.⁵ This error occurred despite the fact that the products differ in marketed strengths [5 mg, 10 mg, and 20 mg vs. 90 mg (at the time the article was published)] as well as dose and frequency of administration (5 mg, 10 mg, 15 mg, or 20 mg once daily vs. 180 mg loading dose followed by 90 mg twice daily (at the time the article was published)).

In addition to the orthographic similarities, both products share overlapping product characteristics, as currently submitted by the Applicant, which increase the potential for wrong drug errors. Both products share the same active ingredient (desmopressin), same indication of use (adult nocturia), same frequency of administration (once nightly before bedtime), and have similar units of measure (mcg/mL vs. mcg). Although a strength will need to be provided for both products, the strengths of Noctiva, 7.5 mcg/mL and [REDACTED]^{(b) (6)} mcg/mL, may be written without the ‘mL’, and scripted orders for Noctiva 7.5 mcg or Noctiva [REDACTED]^{(b) (6)} mcg, may look similar to orders for Nocdurna*** 25 mcg. Although these products have different routes of administration (nasal vs. sublingual), prescribers may omit the route of administration on prescriptions for either product.

We are aware that orthographically similar products with different routes of administration have been confused and have contributed to medication errors due to omission of the route of administration by prescribers. The ISMP Ambulatory Care Newsletter reported a case of confusion between Celebrex and Cerebyx. Celebrex, an oral non-steroidal anti-inflammatory, was ordered as 1000 mg stat by a healthcare provider in an emergency room setting, who actually intended to order Cerebyx, an injectable anti-epileptic agent for a patient with a seizure disorder.⁶ Additionally, ISMP has reported on instances where

⁴ Institute for Safe Medication Practices. Another case of name confusion (what else is [REDACTED]^{(b) (4)}?). ISMP Med Saf Alert. 1998;3(15):1. [REDACTED]^{(b) (4)}.

⁵ Institute for Safe Medication Practices. Safety briefs: Similar drug names confused. ISMP Med Saf Alert Acute Care. 2014;19(12):1-3.

Valtrex (valacyclovir) and Valcyte (valganciclovir) have been confused during prescribing, transcribing and dispensing, resulting in wrong drug errors.⁷ We note that the name pair Valtrex and Valcyte share the same prefix letter string in both the proprietary and established names, and both are used in the clinical setting for similar indications, which is also true for Noctiva and Nocurna***. Given that both names share the same active ingredient, we are concerned that this additional similarity may increase the likelihood that other product characteristics differences may be overlooked.

Given the reasons cited above, we are concerned that if the Noctiva and Nocurna*** name pair is introduced to the marketplace as new therapeutic agents for adult nocturia, especially in a scenario where a short span of time occurs between approvals, practitioners will have difficulty discerning the product characteristics to correctly order these products. Specifically we are aware of wrong drug errors with Farxiga and Fetzima, which may have been potentiated by the drugs being approved within 6 months of one another⁸ despite a combined POCA score of 53%. Considering the product similarities along with post marketing information, we do not think Noctiva and Nocurna*** can safely co-exist in the marketplace. It is difficult to predict the likelihood of adverse effects that may result from confusion between this name pair since they both contain the same active ingredient used for the same indication, however, name confusion between this name pair can result in situations of under dose and over dose given the differences in product strength.

We note that this decision differs from our previous decision. However, previously when this name pair was evaluated in OSE Review RCM #: 2014-26014, the risk for product selection errors during the use of CPOE systems was not considered, nor were the orthographically similar strengths, and overlapping active ingredients, which were factors evaluated in this review and found to be convincing similarities that increase the likelihood of confusion between this name pair.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Bone, Reproductive, and Urologic Products (DBRUP) via e-mail on May 20, 2016. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DBRUP on May 26, 2016, they stated no additional concerns with the proposed proprietary name, Noctiva.

⁶ Institute for Safe Medication Practices. Safety briefs: Cerebyx and Celebrex confusion. ISMP Med Saf Alert Acute Care. 1999; 12(4): 1.

⁷ Institute for Safe Medication Practices. Safety briefs: Valtrex (valacyclovir) and Valcyte (valganciclovir) confusion. ISMP Med Saf Alert Acute Care. 2009;14(17):3.

⁸ Institute for Safe Medication Practices. Safety briefs: Farxiga and Fetzima mix-ups. ISMP Med Saf Alert Acute Care. 2015;20(1):3.

3 REVIEWER'S CONCLUSIONS

The proposed proprietary name is not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with Nocdurna***.

If you have further questions or need clarifications, please contact Shawnetta Jackson, OSE project manager, at 301-796-4952.

3.1 REVIEWER'S COMMENTS REGARDING NOCTIVA

We have completed our review of the proposed proprietary name, Noctiva, and have concluded that this name could result in medication errors due to confusion with another product that is also under review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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

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

Drugs@FDA

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

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.⁹

⁹ 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.
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 medical and/or coined abbreviations in the proprietary name?
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
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 50% 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 $\geq 50\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 49\%$.

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 with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it 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, etc.) may be limited when the strength or dose overlaps. We review 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>	
Y/N	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>	Y/N	Do the names have different number of syllables?
Y/N	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>	Y/N	Do the names have different syllabic stresses?
Y/N	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?	Y/N	Do the syllables have different phonologic processes, such as 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 $\geq 50\%$ 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"> • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	<p>Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.</p>

	Orthographic Checklist (Y/N to each question)	Phonetic Checklist (Y/N to each question)
	<ul style="list-style-type: none"> • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted? 	<ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 49\%$).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA 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. Noctiva Study (Conducted on March 25, 2016)

Handwritten Requisition Medication Order	Verbal Prescription
<p>Medication Order:</p> <p><i>Noctiva (b)(4) One spray into one nostril every evening 30 minutes prior to bedtime</i></p>	<p>Noctiva (b)(4)</p> <p>One spray into one nostril every evening 30 minutes prior to bedtime.</p>
<p>Outpatient Prescription:</p> <p><i>Noctiva 7.5 mcg/mL</i> <i>One spray in either nostril once every evening 30 minutes prior to bedtime.</i></p>	<p>#1</p>

FDA Prescription Simulation Responses

Study Name: Noctiva

285 People Received Study
75 People Responded

Study Name: Noctiva

Total	20	26	29	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
NARCTIVA	0	1	0	1
NATAVA	0	1	0	1
NOCTEVA	0	2	0	2
NOCTIVA	19	20	29	66
NOTEVA	0	1	0	1
NOTIVA	0	1	0	1
VOCTIVA	1	0	0	1

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

No.	<p>Proposed name: Noctiva Established name: Desmopressin acetate Dosage form: Nasal Spray Strength(s): 7.5 mcg/mL and 15 mcg/mL or 0.75 mcg/0.1 mL and 1.5 mcg/0.1mL; or (b) (4) Usual Dose: One spray in one nostril every evening 30 minutes prior to bedtime</p>	<p>POCA Score (%)</p>	<p>Orthographic and/or phonetic differences in the names sufficient to prevent confusion</p> <p>Other prevention of failure mode expected to minimize the risk of confusion between these two names.</p>
1.	Noctiva	100	Proposed proprietary name which is the subject of this review.

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Sustiva	64
2.	Optivar	62
3.	Nexavar	60
4.	Northera	60
5.	(b) (4) ***	60
6.	Raptiva	60
7.	Active Q	59
8.	Certiva	59
9.	Victoza	59
10.	Lexiva	58
11.	Rectiv	58
12.	Ultiva	58
13.	Nacton	58

No.	Name	POCA Score (%)
14.	Natazia	58
15.	Nucala	57
16.	Activase	56
17.	Activella	56
18.	Doctar	56
19.	Moctanin	56
20.	Pexeva	56
21.	Proactiv	56
22.	Tactinal	56
23.	Nioxin	55
24.	Noxafil	55
25.	(b) (4)***	55
26.	Orbactiv	55
27.	Emtriva	54
28.	Naftin	54
29.	Naphcon-A	54
30.	Naquival	54
31.	Neoptic	54
32.	Nexavir	54
33.	Nohist A	54
34.	Notuss AC	54
35.	Novafed A	54
36.	Nocotuss	54
37.	Dactil	53
38.	Factive	53
39.	Natroba	53
40.	Nucynta	53
41.	Octagam	53
42.	Tinactin	53
43.	Vectical	52

No.	Name	POCA Score (%)
44.	Coactin	51
45.	Nelova	51
46.	Nicazel	51
47.	Nuvessa	51
48.	Anectine	51
49.	Atnativ	50
50.	Bacto-Foam	50
51.	Bacti-Free	50
52.	Bacti-Stat	50
53.	Diocetyl	50
54.	Dioclyn	50
55.	Nicotine	50
56.	Nitro IV	50
57.	Noltam	50
58.	Norel LA	50
59.	Norval	50
60.	Novafed	50
61.	Nucochem	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	<p>Proposed name: Noctiva</p> <p>Established name: desmopressin acetate</p> <p>Dosage form: nasal spray</p> <p>Strength(s): 7.5 mcg/mL and 15 mcg/mL mL or 0.75 mcg/0.1 mL and 1.5 mcg/0.1mL; or (b) (4)</p> <p>Usual Dose: Single spray in either nostril each night before bedtime</p>	<p>POCA Score (%)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
1.	<p>(b) (4)***</p>	62	<p>The prefixes and infixes of this name pair have sufficient orthographic differences.</p> <p>The first and second syllables of this name pair have sufficient phonetic differences.</p>
2.	Mectizan	62	<p>The suffixes of this name pair have sufficient orthographic differences</p> <p>The second and third syllables of this name pair sound different.</p>
3.	Natpara	62	<p>The infixes and suffixes of this name pair have sufficient orthographic differences.</p> <p>The second and third syllables of this name pair have sufficient phonetic differences.</p>
4.	Nesina	62	<p>The prefixes and infixes of this name pair have sufficient orthographic differences.</p> <p>The first and second syllables of this name pair have sufficient phonetic differences.</p>
5.	Noctesed	62	<p>The suffixes of this name pair have sufficient orthographic differences.</p> <p>The third syllables of this name pair have sufficient phonetic differences.</p>

No.	<p>Proposed name: Noctiva</p> <p>Established name: desmopressin acetate</p> <p>Dosage form: nasal spray</p> <p>Strength(s): 7.5 mcg/mL and 15 mcg/mL mL or 0.75 mcg/0.1 mL and 1.5 mcg/0.1mL; or (b) (4)</p> <p>Usual Dose: Single spray in either nostril each night before bedtime</p>	POCA Score (%)	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
6.	Nostrilla	62	<p>The infixes and suffixes of this name pair have sufficient orthographic differences.</p> <p>The second syllables of this name pair have sufficient phonetic differences.</p>
7.	(b) (4) ***	62	<p>The prefixes of this name pair have sufficient orthographic differences.</p> <p>The third syllables of this name pair have sufficient phonetic differences.</p>
8.	Ocaliva***	60	<p>The prefixes of this name pair have sufficient orthographic differences.</p> <p>The first and second syllables of this name pair have sufficient phonetic differences.</p> <p>Ocaliva contains an additional syllable which helps differentiate it from Noctiva when spoken.</p>
9.	Boniva	59	<p>The prefixes and infixes of this name pair have sufficient orthographic differences.</p> <p>The first and second syllables of this name pair have sufficient phonetic differences.</p>
10.	Actigall	51	<p>The prefixes and suffixes of this name pair have sufficient orthographic difference.</p> <p>The first, second and third syllables of this name pair have sufficient phonetic differences.</p>

Appendix F: Low Similarity Names (e.g., combined POCA score is $\leq 49\%$)

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

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

No.	Name	POCA Score (%)	Failure preventions
1.	Noctamid	64	Foreign proprietary name available in Germany, Australia, S. Africa, Spain.
2.	(b) (4) ***	60	Proposed proprietary name for NDA 206099 which was approved and marketed under the name Onzetra Xsail.
3.	(b) (4) ***	58	Alternate proposed name for IND (b) (4) Primary name submitted for review was (b) (4) ***. Name found unacceptable and alternate name, (b) (4) *** was submitted. Name found conditionally acceptable in (b) (4)
4.	Pectin	50	Not a proprietary drug name, it is an emulsifying additive for foods and drugs.

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Actemra	50
2.	Amitiza	51
3.	Anexsia	50
4.	Anexsia 5/325	50
5.	Anexsia 7.5/325	50

No.	Name	POCA Score (%)
6.	Anexsia 7.5/650	50
7.	Benerva	50
8.	Decavac	50
9.	Doxidan	52
10.	Droxia	51
11.	Extina	52
12.	Inocor I. V.	52
13.	Menactra	56
14.	Moxeza	62
15.	Ontinua	52
16.	Opdivo	50
17.	Optiray 160	52
18.	Optiray 240	52
19.	Optiray 300	52
20.	Optiray 320	52
21.	Optiray 350	52
22.	Oxecta	52
23.	Pontevia	54
24.	Potiga	51
25.	Sanctura	51
26.	Tarceva	50
27.	Testavan	52
28.	Tibtiba	53
29.	Zostavax	51

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

No.	Name
1.	N/A

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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