

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208411Orig1s000

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:	September 25, 2015
Application Type and Number:	NDA 208411
Product Name and Strength:	Narcan Nasal Spray (naloxone hydrochloride) nasal spray 4 mg per 0.1 mL
Product Type:	Combination product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Adapt Pharma, Inc.
Panorama #:	2015-1000441
DMEPA Primary Reviewer:	Millie Shah, PharmD, BCPS
DMEPA Team Leader:	Vicky Borders-Hemphill, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Narcan Nasal Spray, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by (b)(4) for this product. (b)(4) identified ten sound-alike and/or look-alike product names with Narcan Nasal Spray; however, the overall results of the (b)(4) name safety research support the use of Narcan Nasal Spray as a proposed proprietary name for Adapt Pharma's proposed product for the treatment of opioid overdose. We agree with (b)(4) assessment that these names do not pose a concern.

1.1 REGULATORY HISTORY

Narcan (naloxone hydrochloride injection, USP) Injection was approved on April 13, 1971 (NDA 016636) as a single-dose, (b)(4) pre-filled syringe (0.02 mg/mL, 0.4 mg/mL, and 1 mg/mL) to be administered intravenously, intramuscularly, or subcutaneously. The brand product is no longer marketed in the U.S., but generic alternatives are available.

Adapt Pharma, Inc. acquired both the Narcan proprietary name and rights to the Narcan injection NDA.

1.2 PRODUCT INFORMATION

The Sponsor provided the following product information in the July 20, 2015 proprietary name submission.

- Intended Pronunciation: nar' kan nay' sal spray
- Active Ingredient: naloxone hydrochloride
- Indication of Use: opioid overdose
- Route of Administration: intranasal
- Dosage Form: nasal spray
- Strength: 4 mg per 0.1 mL
- Dose and Frequency: One spray once
- How Supplied: Single nasal spray device packaged in clear blister pack. Carton configurations will include (b)(4) 2 blister packs per carton
- Storage: Room temperature
- Container and Closure Systems: Blister pack

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 Anesthesia, Analgesia, and Addiction Products (DAAAP) 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 name¹.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Narcan Nasal Spray, is derived from, "Narcan is an FDA approved name." This proposed proprietary name is comprised of multiple words that contain the modifier, "Nasal Spray." The Sponsor's intended meaning of the modifier is the nasal spray dosage form. The use of the modifier, "Nasal Spray" does not pose a safety concern because nasal spray is the dosage form.

2.2.3 FDA Name Simulation Studies

Seventy-seven practitioners participated in DMEPA's prescription studies. Of the 77 participants, 73 correctly interpreted the name Narcan Nasal Spray. 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.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE e-mail dated August 7, 2015, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving Narcan that would be relevant for this review.

¹USAN stem search conducted on August 19, 2015.

Table 2. FAERS Search Strategy	
Search Date	July 21, 2015
Drug Name	Narcan [product name]
Event (MedDRA Terms)	DMEPA Official Proprietary Name Review Search Terms Event List: Product name confusion (PT) Medication error (PT) Intercepted medication error (PT) Drug dispensing error (PT) Intercepted drug dispensing error (PT) Circumstance or information capable of leading to a medication error (PT)
Date Limits	All reports through July 1, 2015

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

Our search resulted in 30 reports. After individual review, 28 reports were not included in the final analysis because the cases did not describe possible name confusion between Narcan and another product.

Following exclusions, the search yielded 2 relevant cases. Both cases describe wrong drug errors between Narcan and Norcuron. The outcomes reported in the cases include respiratory depression (n=1) and no harm (n=1). The cases do not provide enough information to determine a root cause. Therefore, it is unclear that the medication error cases can be attributed to look-alike and/or sound-alike name confusion. Furthermore, the proprietary name Norcuron is withdrawn from the market (FR effective July 8, 2011), although generic equivalents of vecuronium bromide are available. The cases of error between Narcan and Norcuron were reported between 1993 and 2003, which is before Norcuron was withdrawn. Based on this information, we do not anticipate look-alike and/or sound-alike name confusion medication errors between Narcan and Norcuron.

2.2.6 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) via e-mail on September 8, 2015. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DAAAP on September 21, 2015, they stated no additional concerns with the proposed proprietary name, Narcan Nasal Spray.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Lisa Skarupa, OSE project manager, at 301-796-2219.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your July 20, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. *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 DNNDP. OPDP or DNNDP 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 DNNDP 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.²

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.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. 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.

- c. 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.

Appendix A1: Description of FAERS

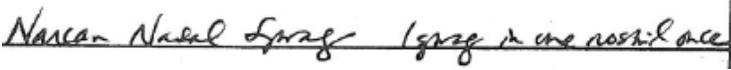
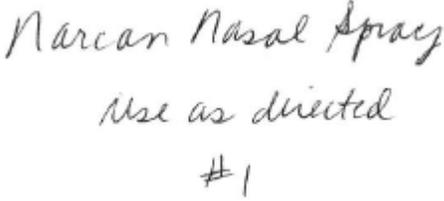
The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International

Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm>.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Narcan Nasal Spray Study (Conducted on August 5, 2015)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Narcan Nasal Spray Use as directed Dispense number one</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

244 People Received Study
77 People Responded

Total	25	25	27	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
??	0	1	0	1
NARAN NASAL SPRAY	0	0	1	1
NARCAN NASAL SPRAY	25	22	26	73
NARCANE NASAL SPRAY	0	1	0	1
NON CAN NASAL SPRAY	0	1	0	1

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/s/

MILLIE C BRAHMBHATT
09/25/2015

BRENDA V BORDERS-HEMPHILL
09/25/2015