CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208411Orig1s006

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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Date of This Review:	March 7, 2023
Application Type and Number:	NDA 208411/S-006
Product Name and Strength:	Narcan (naloxone hydrochloride) nasal spray, 4 mg per 0.1 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Over-the-counter (OTC)
Applicant/Sponsor Name:	Emergent Operations Ireland LTD (Emergent)
PNR ID #:	2023-1044725007
DMEPA 2 Safety Evaluator:	Grace P. Jones, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Naloxone hydrochloride nasal spray, 4 mg per 0.1 mL, was originally approved on November 18, 2015 as a prescription product with the proprietary name Narcan Nasal Spray, under NDA 208411. The Applicant submitted the proprietary name, (b) (4) for naloxone hydrochloride nasal spray, (b) (4) on September 30, 2020 and an amendment on October 26, 2020, which DMEPA found the name acceptable.[a] Of note, (b) (4) (b) (4) was found to be incomplete.

Emergent is now seeking a full prescription to nonprescription switch for naloxone hydrochloride nasal spray, 4 mg per 0.1 mL, under NDA 208411/S-006, for the nonprescription indication, for the emergency treatment of an opioid overdose.

Thus, Emergent submitted the proposed proprietary name, Narcan, for review on February 24, 2023.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 24, 2023.

- Intended Pronunciation: nar' kan
- Active Ingredient: naloxone hydrochloride
- Indication of Use: opioid overdose
    - Drug Facts Label (DFL) *Uses*:

      Uses

      - to "revive" someone during an overdose from many **prescription pain medications** or **street drugs such as heroin**
      - this medicine can save a life
- Route of Administration: intranasal
- Dosage Form: nasal spray

[a] Myers D. Proprietary Name Review for (b) (4) (NDA 208411). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 JAN 22. PNR ID No. 2020-43330540.

- Strength: 4 mg per 0.1 mL
- Dose and Frequency: One 0.1 mL 4 mg spray, single dose, administered every 2-3 minutes, as needed for the treatment of opioid overdose
    - DFL *Directions*:

(b) (4)

- How Supplied: carton containing 2 clear blister packages, each containing a single nasal spray device and a Quick Start Guide
- Storage: (b) (4)

- DFL *Other information*:

  store below 25°C (77°F), do not freeze, avoid excessive heat above 40°C (104°F)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT & COMMENTS FROM THE REVIEW DISCIPLINE AT INITIAL REVIEW

At the initial phase of the review, the Division of Nonprescription Drugs I (DNPD I) indicated that they have no objections to the proposed proprietary name, Narcan. We concur with DNPD I's assessment at initial review and find that the proposed proprietary name, Narcan, would not misbrand the proposed product.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Emergent indicated in their submission that the proposed proprietary name, Narcan, is derived from the approved name for naloxone hydrochloride nasal spray, Narcan Nasal Spray, and the product is commonly referred to as Narcan. 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 can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Seventy-nine practitioners participated in DMEPA's prescription studies for Narcan. Three practitioners from the inpatient written name simulation study added the words, nasal spray. In this instance, users would receive Narcan Nasal Spray, which is the exact same product; thus, the residual risk of product confusion is acceptable in this case. The remaining responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

[b] USAN stem search conducted on February 21, 2023.

2.2.4 Safety Analysis of the Proposed Proprietary Name, Narcan

The proposed nonprescription product contains the same active ingredient as the prescription Narcan Nasal Spray. Emergent proposes to market the nonprescription product with the proprietary name, Narcan, omitting the modifier, nasal spray.

We note that naloxone hydrochloride injection, USP (NDA 016636) in prefilled syringe, vial, and ampule presentations used to be marketed under the proprietary name Narcan. The brand Narcan injection products were already no longer marketed in the U.S. before the approval of prescription Narcan Nasal Spray in 2015. However, generic equivalents to Narcan injection products are available at the time of this review and prescribers may still prescribe them using the brand name Narcan, thus, the removal of "nasal spray" in the proprietary name for the proposed nonprescription product may introduce risk of wrong dosage form errors (e.g., misinterpret an order for Narcan intended for the nasal spray dosage form as Narcan injection). On the other hand, it is common nomenclature practice to market multiple dosage forms under the same proprietary name (e.g., Claritin, Renvela, Pradaxa). From our medication safety experience gained through routine post-market surveillance, prescribers may indicate the dosage form on a prescription to specify the intended dosage form when multiple dosage forms are marketed under the same name. We anticipate a prescription for the proposed nonprescription product to specifically indicate nasal spray on the prescription (e.g., prescriber will include the dosage form, or indicate the nasal route of administration via the sig) as this is observed from the FDA simulated name study where three practitioners from the inpatient written name portion of the study added the words "nasal spray" in their response to the study name "Narcan".

Furthermore, we note that "nasal spray" is described throughout the proposed nonprescription product's labels and labeling and is part of the statement of identity, which is prominently located after the established name on the Principal Display Panel (PDP) of the labels and labeling. Adequate labels and labeling will communicate the dosage form and the nasal route of administration to the user, and help to mitigate the risk of medication errors associated with use of the Narcan injection and nasal spray as well.

Given that Narcan Nasal Spray has been marketed as a prescription product, we also leaned on our routine post-market surveillance. We have not identified medication error concerns of product name confusion related to Narcan Nasal Spray from our routine post-market surveillance.

Therefore, the use of the proposed proprietary name, Narcan, for the proposed nonprescription naloxone hydrochloride nasal spray product is acceptable.

2.2.5 Communication of DMEPA's Determination

On March 7, 2023, DMEPA 2 communicated our determination to the Division of Nonprescription Drugs I (DNPDI).

3 CONCLUSION

The proposed proprietary name, Narcan, is conditionally acceptable.

If you have any questions or need clarifications, please contact Abiola Olagundoye-Alawode, OSE project manager, at 301-796-3982.

3.1 COMMENTS TO EMERGENT OPERATIONS IRELAND LTD

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

If any of the proposed product characteristics as stated in your submission, received on February 24, 2023, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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. 6F[c]

*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.

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

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.

   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.

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.

   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 B: Prescription Simulation Samples and Results

Figure 1. Narcan Study (Conducted on February 24, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: Narcan Give nasal spray now	Narcan Use as directed Dispense 1 carton
Outpatient Prescription: Narcan Use as directed #1 carton	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Narcan	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Narcan

257 People Received Study
79 People Responded

Study Name: Narcan

Total	20	18	18	23	
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
NARCAN	17	18	18	23	76
NARCAN NASAL SPRAY	3	0	0	0	3

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.

/s/

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