# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 205920Orig1s000

# 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:** | August 22, 2018 |
| **Application Type and Number:** | NDA 205920 |
| **Product Name and Strength:** | Primatene Mist (Epinephrine) Inhalation Aerosol, 125 mcg per inhalation |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | OTC |
| **Applicant/Sponsor Name:** | Armstrong Pharmaceuticals, Inc. |
| **Panorama #:** | 2018-23607591 |
| **DMEPA Safety Evaluator:** | Grace P. Jones, PharmD, BCPS |
| **DMEPA Team Leader:** | Chi-Ming (Alice) Tu, PharmD, BCPS |
| **DMEPA Deputy Director:** | Danielle Harris, PharmD, BCPS |

Contents

# 1 INTRODUCTION

This review evaluates the proposed proprietary name, Primatene Mist, 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

Primatene Mist (epinephrine) inhalation aerosol was approved on November 8, 1967, under NDA 016126 and was originally marketed by Wyeth Consumer Healthcare. Armstrong Pharmaceuticals, Inc., had been the contract manufacturer of Primatene Mist for Wyeth from 2004 to 2008. On July 8, 2008, the Applicant Armstrong Pharmaceuticals, Inc. acquired Primatene Mist (epinephrine) inhalation aerosol from Wyeth and marketed the product until December 31, 2011, when it was withdrawn from distribution due to the phase out of chlorofluorocarbons (CFC) outlined in the Montreal Protocol. Since then, the Applicant has re-formulated the epinephrine inhalation aerosol using HFA-134a (hydrofluoroalkane) as the propellant under IND 074286.

On December 11, 2013, the Applicant submitted the proposed proprietary name, (b) (4) for their proposed reformulated product, epinephrine inhalation aerosol, under NDA 205920 which was later amended on April 16, 2014, to request the proposed proprietary name, (b) (4) However, on May 22, 2014, the application received a Complete Response action letter, thus, the review of the proposed proprietary name (b) (4) was terminated (See DARRTS communication dated 6/17/2014).

On June 28, 2016, the Applicant resubmitted their application under NDA 205920 for the proposed reformulated product, epinephrine inhalation aerosol. On June 30, 2016, they resubmitted the proposed proprietary name (b) (4) for review. The Division of Nonprescription Drug Products (DNDP) (b) (4) On September 14, 2016, DMEPA held a teleconference with the Applicant (see DARRTS communication dated 10/28 /2016) to communicate these concerns and provide some alternative recommendations for the Applicant to consider.

The Applicant submitted the proposed proprietary name, Primatene Mist***, on September 19, 2016 under NDA 205920. We found the name, Primatene Mist***, acceptable on November 1, 2016.[a] However, the application received a Complete Response (CR) on December 23, 2016.

On May 7, 2018, the Applicant resubmitted their application under NDA 205920 for the proposed product, epinephrine inhalation aerosol. On June 6, 2018, they resubmitted the proposed proprietary name, Primatene Mist, for review.

[a] Jones, G. Proprietary Name Review for Primatene Mist (NDA 205920). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 NOV 01. Panorama No. 2016-10269700.

### 1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on June 6, 2018. The labels and labeling were submitted in the resubmission received on May 7, 2018.

- Intended Pronunciation: ˈprī-mə-tēn ˈmist
- Active Ingredient: Epinephrine
- Indication of Use: Drug Facts Label (DFL) Uses:
    - For temporary relief of mild symptoms of intermittent asthma
        - wheezing
        - tightness of chest
        - shortness of breath
- Route of Administration: Oral inhalation
- Dosage Form: Aerosol
- Strength: 0.125 mg per inhalation
- Dose and Frequency: DFL Directions:
    - For adults and children 12 years of age and over.
    - Children under 12 years of age: do not use; it is not known if the drug works or is safe in children under 12.
    - Start with one inhalation. Wait 1 minute. If symptoms not relieved, take a second inhalation.
    - Wait at least 4 hours between doses.
    - Do not use more than 8 inhalations in 24 hours.
- How Supplied: Container of 160 inhalations
- Storage: Store at room temperature, between 15-25°C (59-77°F)

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT & INITIAL COMMENTS

At the initial phase of the review, in response to our initial OSE, June 27, 2018 email, the Division of Nonprescription Drug Products (DNDP) had no concerns relating to the proposed proprietary name, Primatene Mist. DMEPA concurs with DNDP's assessment at initial review and concludes that the proposed proprietary name does not misbrand the proposed product.

### 2.2 SAFETY ASSESSMENT

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

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

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

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

The Applicant indicated in their submission that the proposed name, Primatene Mist, is a legacy name that was used for the original chlorofluorocarbon (CFC) propellant containing Primatene Mist product. The Applicant further indicated that the root name, Primatene, is derived from the pair of asthma products (the tablets and inhalation spray) used for the temporary relief of symptoms of intermittent asthma, and the modifier Mist designates the dosage form and differentiates the proposed inhalation aerosol formulation product from the tablets.

This proprietary name is comprised of multiple words, the root name, Primatene, and the modifier Mist. We further discuss our assessment of the proposed proprietary name, Primatene Mist, in Section 2.2.5.

### *2.2.3 FDA Name Simulation Studies*

Sixty-seven 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.

### *2.2.4 Medication Error Data Selection of Cases*

As part of our re-assessment of the proposed proprietary name, Primatene Mist, we conducted a gap FDA Adverse Event Reporting System (FAERS) database search to ensure that no recent post-marketing experience would alter our previous conclusion of acceptability of the proposed proprietary name, Primatene Mist.

Our FAERS search used the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Primatene and Primatene Mist*** that would be relevant for this review.

**Table 2. FAERS Search Strategy**

| | |
|---|---|
| **Search Date** | July 27, 2018 |
| **Drug Name** | Primatene [product name] and Primatene Mist [product name] |
| **Event (MedDRA Terms)** | **DMEPA Official PNR Name Confusion Search Terms Event List:**<br>Preferred Terms:<br>CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR<br>DRUG ADMINISTRATION ERROR<br>DRUG DISPENSING ERROR<br>DRUG PRESCRIBING ERROR |

[b] USAN stem search conducted on June 26, 2018.

| Table 2. FAERS Search Strategy | |
|---|---|
| | INTERCEPTED DRUG DISPENSING ERROR<br>INTERCEPTED DRUG PRESCRIBING ERROR<br>INTERCEPTED MEDICATION ERROR<br>MEDICATION ERROR<br>PRODUCT NAME CONFUSION<br>TRANSCRIPTION MEDICATION ERROR<br>Lower Level Terms:<br>INTERCEPTED PRODUCT SELECTION ERROR<br>INTERCEPTED WRONG DRUG PRODUCT SELECTED<br>INTERCEPTED WRONG DRUG SELECTED<br>PRODUCT SELECTION ERROR<br>WRONG DEVICE DISPENSED<br>WRONG DRUG ADMINISTERED<br>WRONG DRUG DISPENSED<br>WRONG DRUG PRESCRIBED<br>WRONG DRUG PRODUCT SELECTED<br>WRONG DRUG SELECTED<br>WRONG PRODUCT SELECTED |
| **Date Limits** | Gap Search: September 17, 2016 to July 27, 2018 (from the date of the FAERS search in the previous Primatene Mist name review[c] to current search date) |

The gap FAERS search did not retrieve any cases. The previous name review FAERS search also did not identify any medication error reports of product name confusion related to Primatene Mist. Thus, we maintain our previous assessment of finding no safety concerns with the proposed proprietary name, Primatene Mist.

### *2.2.5 Evaluation of the Proposed Proprietary Name, Primatene Mist*

The proposed epinephrine inhalation product is proposed for OTC use to temporarily relieve mild symptoms of intermittent asthma in adults and children 12 years of and older. Additionally, all product characteristics remain the same when comparing the current June 6, 2018 submission and previous September 19, 2016 name submission. For re-assessment of the proposed proprietary name, Primatene Mist, we conducted a gap FAERS search and searched the USAN stem list, which further confirmed no reports of name confusion and no USAN stems in the proposed proprietary name. Our re-assessment did not identify any new concerns that represent a potential source of drug name confusion. Furthermore, we refer to our previous review[d] and assessment of the proposed proprietary name, Primatene Mist, and our

[c] Jones, G. Proprietary Name Review for Primatene Mist (NDA 205920). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 NOV 02. Panorama No. 2016-10269700.

[d] Jones, G. Proprietary Name Review for Primatene Mist (NDA 205920). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 NOV 02. Panorama No. 2016-10269700.

determination that the name was acceptable for this proposed product. In this current review, we maintain our determination that the proposed proprietary name is acceptable.

#### *2.2.6 Communication of DMEPA's Analysis at Midpoint of Review of the Proposed Proprietary Name, Primatene Mist*

DMEPA communicated our findings to the Division of Nonprescription Drug Products (DNDP) via e-mail on August 16, 2018. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DNDP on August 22, 2018, they stated no additional concerns with the proposed proprietary name, Primatene Mist.

## 3 CONCLUSION

The proposed proprietary name is 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 THE APPLICANT

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

If any of the proposed product characteristics as stated in your submission, received on June 6, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

## 4 REFERENCES

***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.

***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. [e]

[e] 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 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 B:** Prescription Simulation Samples and Results

**Figure 1. Primatene Mist Study (Conducted on June 19, 2018)**

| Handwritten Medication Order/Prescription | Verbal Prescription |
|---|---|
| Medication Order:<br>Primatene Mist 1 inhalation now, may repeat in 1 minute. Wait 4 hrs between doses. | Primatene Mist<br>Use as directed<br>Dispense #1 |
| Outpatient Prescription:<br>Primatene Mist<br>Use as directed<br># 1 | |

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

307 People Received Study

67 People Responded

| **Total** | **25** | **19** | **23** | |
|---|---|---|---|---|
| **INTERPRETATION** | **OUTPATIENT** | **VOICE** | **INPATIENT** | **TOTAL** |
| PREMATENE MIST | 1 | 0 | 0 | 1 |
| PREMATINE MIST | 1 | 0 | 0 | 1 |
| PRIMATENE | 0 | 0 | 1 | 1 |
| PRIMATENE MIST | 20 | 13 | 20 | 53 |
| PRIMATESE MIST | 2 | 0 | 0 | 2 |
| PRIMATINE MIST | 1 | 3 | 1 | 5 |
| PRIMATINE MYST | 0 | 0 | 1 | 1 |
| PRIMETINE MIST | 0 | 1 | 0 | 1 |
| PRIMITINE MIST | 0 | 1 | 0 | 1 |
| TYLETINE MIST | 0 | 1 | 0 | 1 |

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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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GRACE JONES
08/22/2018

CHI-MING TU
08/22/2018

DANIELLE M HARRIS
08/23/2018

**PROPRIETARY NAME REVIEW**

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| | |
|---|---|
| **Date of This Review:** | November 1, 2016 |
| **Application Type and Number:** | NDA 205920 |
| **Product Name and Strength:** | Primatene Mist (Epinephrine) Inhalation Aerosol, 125 mcg per inhalation |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | OTC |
| **Applicant/Sponsor Name:** | Armstrong Pharmaceuticals, Inc. |
| **Panorama #:** | 2016-10269700 |
| **DMEPA Primary Reviewer:** | Grace P. Jones, PharmD, BCPS |
| **DMEPA Team Leader:** | Chi-Ming (Alice) Tu, PharmD |
| **DMEPA Acting Associate Director:** | Danielle Harris, PharmD, BCPS |
| **DMEPA Division Director:** | Todd Bridges, RPh |

Contents

# 1 INTRODUCTION

This review evaluates the proposed proprietary name, Primatene Mist, 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

Primatene Mist (epinephrine) inhalation aerosol was approved on November 8, 1967, under NDA 016126 and was originally marketed by Wyeth Consumer Healthcare. Armstrong Pharmaceuticals, Inc., had been the contract manufacturer of Primatene Mist for Wyeth from 2004 to 2008. On July 8, 2008, the Applicant Armstrong Pharmaceuticals, Inc. acquired Primatene Mist (epinephrine) inhalation aerosol from Wyeth and marketed the product until December 31, 2011, when it was withdrawn from distribution due to the phase out of chlorofluorocarbons (CFC) outlined in the Montreal Protocol. Since then, the Applicant has re-formulated the epinephrine inhalation aerosol using HFA-134a (hydrofluoroalkane) as the propellant under IND 074286.

On December 11, 2013, the Applicant submitted the proposed proprietary name, (b) (4) for their proposed reformulated product, epinephrine inhalation aerosol, under NDA 205920 which was later amended on April 16, 2014, to request the proposed proprietary name, (b) (4) However, on May 22, 2014, the application received a Complete Response action letter, thus, the review of the proposed proprietary name (b) (4) was terminated (See DARRTS communication dated 6/17/2014).

On June 28, 2016, the Applicant resubmitted their application under NDA 205920 for the proposed reformulated product, epinephrine inhalation aerosol. On June 30, 2016, they resubmitted the proposed proprietary name (b) (4) for review. The Division of Nonprescription Drug Products (DNDP) (b) (4) On September 14, 2016, DMEPA held a teleconference with the Applicant (see DARRTS communication dated 10/28/2016) to communicate these concerns and provide some alternative recommendations for the Applicant to consider. Thus, on September 19, 2016, the Applicant submitted the currently proposed proprietary name, Primatene Mist, for review.

## 1.2 PRODUCT INFORMATION

The following product information is provided in the September 19, 2016 proprietary name submission.

- Intended Pronunciation: ˈprī-mə-tēn ˈmist
- Active Ingredient: Epinephrine
- Indication of Use: For temporary relief of mild symptoms of intermittent asthma
- Route of Administration: Oral inhalation

- Dosage Form: Aerosol
- Strength: 0.125 mg per inhalation
- Dose and Frequency:
    - Adults and children 12 years of age and over: 1 to 2 inhalations for each dose. Start with one inhalation, wait at least 1 minute. If not relieved, use once more. Wait at least 4 hours between doses. Do not use more than 8 inhalations in 24 hours.
    - Children under 12 years of age: do not use; it is not known if the drug works or is safe in children under 12.
- How Supplied: Container of 160 inhalations
- Storage: Store at room temperature, between 15-25°C (59-77°F)

## 2 RESULTS

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

### 2.1 SAFETY ASSESSMENT

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

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

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

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

The Applicant indicated in their submission that the proposed name, Primatene Mist, is the name used for the original Primatene Mist product containing the CFC propellant. Although the inhalation (CFC propellant) product has been discontinued, the Applicant also indicated the root name Primatene is derived from the pair of asthma products used for temporary relief of symptoms of intermittent asthma for tablets and inhalation spray, whereby the modifier Mist designates the inhalation aerosol formulation. We further discuss our assessment of the name Primatene Mist in Section 2.1.4 and 2.1.5.

#### *2.1.3 FDA Name Simulation Studies*

Ninety-seven practitioners participated in DMEPA's prescription studies. Seventy-seven practitioners responded with the correct interpretation of the proposed name, Primatene Mist. 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.

[a] USAN stem search conducted on October 5, 2016.

### *2.1.4 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 ***Primatene and Primatene Mist*** that would be relevant for this review.

| **Table 2. FAERS Search Strategy** | |
|---|---|
| **Search Date** | September 17, 2016 |
| **Drug Name** | Primatene [product name]<br>Primatene Mist [product name] |
| **Event (MedDRA Terms)** | **DMEPA Official PNR Name Confusion Search Terms Event List:**<br>Preferred Terms:<br>CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR<br>DRUG ADMINISTRATION ERROR)<br>DRUG DISPENSING ERROR<br>DRUG PRESCRIBING ERROR<br>INTERCEPTED DRUG DISPENSING ERROR<br>INTERCEPTED DRUG PRESCRIBING ERROR<br>INTERCEPTED MEDICATION ERROR<br>MEDICATION ERROR<br>PRODUCT NAME CONFUSION<br>TRANSCRIPTION MEDICATION ERROR<br>Lower Level Terms:<br>INTERCEPTED PRODUCT SELECTION ERROR<br>INTERCEPTED WRONG DRUG PRODUCT SELECTED<br>INTERCEPTED WRONG DRUG SELECTED<br>PRODUCT SELECTION ERROR<br>WRONG DEVICE DISPENSED<br>WRONG DRUG ADMINISTERED<br>WRONG DRUG DISPENSED<br>WRONG DRUG PRESCRIBED<br>WRONG DRUG PRODUCT SELECTED<br>WRONG DRUG SELECTED<br>WRONG PRODUCT SELECTED |
| **Date Limits** | No date limit |

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.

The search yielded 13 cases (one reported in 2001, 10 reported in 2002, one reported in 2003, and one reported in 2008). All 13 cases were not included in the final analysis for the following

reasons: wrong technique, overdose, lack of information provided, cases related to drug misuse and abuse, and a case describing use of Primatene Mist as advised by OBGYN provider and patient delivered a child with birth defects; no other information was provided in this case.

Our FAERS search did not identify any medication error reports of product name confusion related to the names Primatene or Primatene Mist. Of note, no name confusion or product confusion was found between the Primatene (Ephedrine/Guaifenesin) tablets and the Primatene Mist (Epinephrine) aerosol (See discussion in Section 2.1.5). Therefore, our FAERS search did not find any safety concerns with the proposed proprietary name Primatene Mist.

### *2.1.5 Evaluation of the proposed proprietary name, Primatene Mist*

Primatene Mist (Epinephrine) aerosol had been marketed as an OTC product since the 1960s for the temporarily relief of mild symptoms of intermittent asthma; however, since it contained the CFC propellant, Primatene Mist was phased out of the market at the end of 2011 due to the Montreal Protocol.

Primatene (Ephedrine/Guaifenesin) tablets, albeit a monograph product, has been marketed as an OTC product since the 1950s. Primatene tablets are now stored in locked cabinets or behind the counter since September 2006 per the Combat Methamphetamine Epidemic Act of 2005.

As a part of the submission for the proposed proprietary name Primatene Mist, the Applicant provided justification that Primatene Mist aerosol and Primatene tablets had coexisted in the OTC marketplace for over 40 years between 1967 and 2011 before Primatene Mist's discontinuation in 2011. Additionally, the Applicant estimated that between 2004 and 2011, (b) (4) of Primatene tablets and (b) (4) of Primatene Mist were sold in the marketplace, and during this time period, there were no reports of medication error due to consumer product confusion or anecdotal reports of confusion between Primatene Mist and Primatene tablets. Our FAERS search also did not identify any confusion (see Section 2.1.4). Moreover, Primatene tablets will be located behind the pharmacy counter and will not be in close proximity to Primatene Mist on pharmacy shelves.

Although we recommend against the use of the same root name when products do not contain at least one common active ingredient, in this specific instance with Primatene Mist, we do not object to the use of Primatene in the name because:

1. There is a long history of over 40 years of both products having been co-marketed without product name confusion errors as noted by the Applicant.
2. Our FAERS search also did not identify any medication error reports of product name confusion related to the names Primatene Mist and Primatene.
3. The use of the name Primatene Mist may help convey to previous users of the original product that the active ingredient in this reformulated proposed product is the same active ingredient as in the original product.

In regards to the potential concern that the proposed name Primatene Mist may mislead consumers to think the operating instructions for the proposed HFA product are the same as the original CFC product, 5 years have elapsed since the CFC product's discontinuation so the risk of such confusion is lower than when the CFC product was first discontinued. Furthermore,

product labeling can help address the risk of consumers thinking they can use this HFA product the same way as the CFC product. Additionally, the device for the HFA product is a very different device compared to the CFC device. The different look and feel of the device for the HFA product will also signal to consumers that this proposed HFA product device is not the same as the original CFC product.

Therefore, for the aforementioned reasons, we find the proposed proprietary name is acceptable for this proposed product.

## 3 CONCLUSIONS

The proposed proprietary name is 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 THE APPLICANT

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

If any of the proposed product characteristics as stated in your September 19, 2016 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

## 4 REFERENCES

***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.

***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).

***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. [b]

[b] 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. 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. Primatene Mist Study (Conducted on September 30, 2016)**

| Handwritten Medication Order/Prescription | Verbal Prescription |
|---|---|
| Medication Order:<br>Primatene Mist 1 puff now, may repeat in 4 hrs if needed<br>Outpatient Prescription:<br>Primatene Mist<br>Use as Directed | Primatene Mist<br>Use as directed<br>Dispense #1 |

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

309 People Received
Study
97 People Responded

Study Name: Primatene Mist

| **Total** | **29** | **30** | **38** | |
|---|---|---|---|---|
| **INTERPRETATION** | **OUTPATIENT** | **VOICE** | **INPATIENT** | **TOTAL** |
| PRAMITENE MIST | 0 | 1 | 0 | 1 |
| PREMINTIN MIST | 0 | 1 | 0 | 1 |
| PRIMANTENE MIST | 0 | 0 | 1 | 1 |
| PRIMATENE | 1 | 0 | 0 | 1 |
| PRIMATENE MIST | 25 | 20 | 32 | 77 |
| PRIMATERANTIST | 0 | 0 | 1 | 1 |
| PRIMATERE MIST | 0 | 0 | 2 | 2 |
| PRIMATEREMIST | 0 | 0 | 1 | 1 |
| PRIMATIN MIST | 0 | 1 | 0 | 1 |
| PRIMATINE MIST | 0 | 6 | 1 | 7 |
| PRIMATME MIST | 1 | 0 | 0 | 1 |
| PRIMATRNR MIST | 1 | 0 | 0 | 1 |
| PRIMETINE MIST | 0 | 1 | 0 | 1 |
| PRIVATENE MIST | 1 | 0 | 0 | 1 |

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

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/s/

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