CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211358Orig1s000

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:	February 27, 2018
Application Type and Number:	IND 079521 and NDA 211358
Product Name and Strength:	Orkambi (lumacaftor and ivacaftor) Oral Granules 100 mg/125 mg and 150 mg/188 mg
Product Type:	Multi-Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Vertex Pharmaceuticals
Panorama #:	2017-19396798 and 2018-20951699
DMEPA Safety Evaluator:	Lissa C. Owens, PharmD
DMEPA Team Leader:	Sarah K. Vee, PharmD
DMEPA Associate Director:	Mishale Mistry, PharmD, MPH

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Orkambi, 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 proposed proprietary name.

1.1 REGULATORY HISTORY

Orkambi (lumacaftor and ivacaftor) tablets, 100 mg/125 mg and 200 mg/125 mg, was approved on July 2, 2015 under NDA 206038 and is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the F508del mutation in the CFTR gene.

On November 30, 2017, the Applicant submitted IND 079521 and on February 7, 2018, the Applicant submitted NDA 311358, which proposes lumacaftor and ivacaftor oral granules under the proprietary name Orkambi.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submissions received on November 30, 2017 and February 7, 2018, and DailyMed.

Table 2. Relevant Product Information for Orkambi

Product Name	**Orkambi**	**Orkambi**
Initial Approval Date	July 2, 2015	N/A – proposed product
Active Ingredient	lumacaftor and ivacaftor	
Indication	Treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the F508del mutation in the CFTR gene.	Treatment of cystic fibrosis (CF) in patients age 2 years through 5 years who are homozygous for the F508del mutation in the CFTR gene.
Route of Administration	Oral	
Dosage Form	Tablet	Granules
Strength	100 mg/125 mg and 200 mg/125 mg	100 mg/125 mg and 150 mg/188 mg
Dose and Frequency	• Ages 6 through 11 years: 2 lumacaftor 100 mg/ivacaftor 125 mg tablets every 12 hours (total daily dose: lumacaftor 400 mg/ivacaftor 500 mg) • Ages 12 years and older: 2 lumacaftor 200 mg/ivacaftor 125 mg tablets every 12 hours (total daily dose: lumacaftor 800 mg/ivacaftor 500 mg)	• Less than 14 kg: 1 packet of 100 mg/125 mg lumacaftor/ivacaftor every 12 hours (total daily dose: lumacaftor 200 mg/ivacaftor 250 mg) • 14 kg or greater: 1 packet of 150 mg/188 mg lumacaftor/ivacaftor every 12 hours (total daily dose: lumacaftor 300 mg/ivacaftor 376 mg)
How Supplied	112–count tablet box containing a 4-week supply (4 weekly cartons of 7	Carton contains 4 individual wallets. Wallets contain 14 packets. 56 count

	daily blister strips with 4 tablets per strip)	packets
Storage	20°C -25°C (68°F -77°F) with excursions permitted to 15°C-30°C (59-86°F)	

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. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) 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 name[a].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Orkambi 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 Comments from Other Review Disciplines at Initial Review

In response to the OSE, December 26, 2017 e-mail, the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 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 ***Orkambi*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	February 6, 2018
Drug Name	Orkambi [product name]

[a] USAN stem search conducted on February 6, 2018

Table 2. FAERS Search Strategy	
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	No date limitation

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.

After individual review; following exclusions, the search did not yield any relevant cases.

2.2.5 Multiple Dosage Forms Under a Single Proprietary Name

Under IND 079521 and NDA 211358, the Applicant proposes a new oral dosage form of lumacaftor and ivacaftor for oral granules, in strengths of 100 mg/125 mg and 150 mg/188 mg, to be marketed under the same proprietary name as the currently approved product, Orkambi. The Applicant proposes to market the dosage form of oral granules to facilitate drug administration in pediatric patient's ages 2 to 5 years.

We note that Orkambi is currently available in 100 mg/125 mg and 200 mg/125 mg tablets and shares the same active ingredients, indication (treatment of cystic fibrosis in patients who are

homozygous for the F508del mutation in the CFTR gene), route of administration and frequency as the proposed oral granules formulation. We note that the two dosage forms will share strength of 100 mg/125 mg. We note that the Applicant conducted a bioavailability study in healthy volunteers to compare the oral granules and tablets. The Applicant stated that the relative bioavailability was comparable between both granules and tablets and the *lumacaftor* and *ivacaftor* exposures were dose proportional between both granules formulations (i.e. *lumacaftor* 100-mg/*ivacaftor*125-mg and *lumacaftor* 150-mg/*ivacaftor*188-mg doses). Given the overlapping strength and the potential for the oral tablet and oral granules to be substituted for one another in practice, we consulted the DPARP review team with regards to whether the dosage forms are equivalent on a mg per mg basis. Per the Office of Pharmaceutical Quality (OPQ) reviewer, the 100 mg/125 mg strength in both dosage forms is equivalent on a mg-by-mg basis. Per the clinical reviewer, the proposed oral granules and marketed tablets are equivalent on a mg-to-mg basis. Therefore, the risk of dosing errors due to converting between dosage forms is mitigated.

It is a common and accepted practice to have a product line with multiple dosage forms managed under one proprietary name within a single package insert. In this case, the residual risk of confusion between the lumacaftor and ivacaftor oral granules and tablet formulations of the product may be mitigated through labels and labeling intervention and the different age indications for the products. Moreover, we have not identified any relevant medication errors involving name confusion with the proprietary name Orkambi. Therefore, we find the Applicant's proposal to market the proposed product with the proprietary name Orkambi acceptable.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on February 22, 2018. At that time, we also requested additional information or concerns that could inform our review. They stated no additional concerns with the proposed proprietary name, Orkambi.

3 CONCLUSION

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Michael Sinks, OSE project manager, at 240-402-2684.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your submission, received on November 30, 2017 or February 7, 2018 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.

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]

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.

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[b] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

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/s/

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