CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214770Orig1s000

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:	April 30, 2021
Application Type and Number:	NDA 214770
Product Name and Strength:	Noxafil PowderMix (posaconazole) for delayed-release oral suspension, 300 mg per packet
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (Merck)
PNR ID #:	2021-10447273792
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Team Leader (Acting):	Valerie S. Vaughan, PharmD

Contents

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Merck intends to extend their Noxafil product line to include a new for delayed-release oral suspension formulation. The root name, Noxafil, was originally approved on September 15, 2006. The current product line includes:

- Noxafil (posaconazole) oral suspension, 40 mg/mL (NDA 022027);
- Noxafil (posaconazole) tablets, delayed-release, 100 mg (NDA 205053); and
- Noxafil (posaconazole) injection, 300 mg/16.7 mL (18 mg/mL) (NDA 205596).

Merck intends to introduce a new, for delayed-release oral suspension, formulation of posaconazole. Merck proposes to market the new formulation under the one Noxafil prescribing information along with the other formulations of Noxafil. Of note, the new proposed formulation is not bioequivalent on a mg to mg basis with the currently marketed oral suspension formulation. At the initial phase of name review, we were concerned the use of the root name alone could result in product selection error between Noxafil oral suspension and Noxafil for delayed-release oral suspension. Thus, on October 30, 2020, we held a teleconference with Merck to express our concern for product selection error with the proposed proprietary name. During the teleconference, Merck expressed that they would await the Agency's completed review and determination letter of the proposed proprietary name. Thus, on November 3, 2020 we found the use of the root name alone unacceptable because the proposed proprietary name does not distinguish the proposed posaconazole for delayed-release oral suspension formulation from the currently marketed oral suspension product formulation, which could lead to wrong dose errors.[a]

Subsequently, on February 2, 2021, Merck submitted the name Noxafil PowderMix for review.

[a] Myers, D. Proprietary Name Review for Noxafil (NDA 214770). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 03. Panorama No. 2020-41831928.

On February 12, 2021, Merck submitted an Amendment to Proprietary Name Request response to our February 5, 2021, email communication indicating that their February 2, 2021, Request for Proprietary Name Review was incomplete.[b,c,d]

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 2, 2021 and subsequent Amendment received on February 12, 2021, that cross references supporting labeling documents submitted as part of the efficacy supplement submitted to NDA 205596 on February 12, 2021.

Table 1. Relevant Product Information for Noxafil (NDAs 214770, 022003, 205053, and 205596)

	Noxafil PowderMix	**Noxafil**		
Application No.	**NDA 214770**	**NDA 022003**	**NDA 205053**	**NDA 205596**
Approval Date	Not Applicable	09/15/2006	11/25/2013	03/13/2014
Intended Pronunciation	NOX-a-fil paw-der miks	NOX-a-fil		
Active Ingredient	posaconazole			
Dosage Form	for delayed-release oral suspension	Oral Suspension	Tablets, Delayed-release	Injection
Indication of Use[e]	In patients 2 years of age and older for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-			

[b] Cover Letter: Amendment to Request for Proprietary Name Review for Noxafil PowderMix (NDA 214770). Whitehouse Station (NJ): Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; 2021 FEB 21. Available at: \\CDSESUB1\evsprod\nda214770\0017\m1\us\cover-letter.pdf.

[c] Amendment to Request for Proprietary Name Review for Noxafil PowderMix (NDA 214770). Whitehouse Station (NJ): Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; 2021 FEB 21. Available at: \\CDSESUB1\evsprod\nda214770\0017\m1\us\proprietary-names.pdf.

[d] Miles, N. FDA Communication: NDA 214770 – Noxafil PFS – submission of proprietary name request: FDA, CDER, OND, DAI (US); 2021 FEB 05. Available from: https://darrts fda.gov/darrts/faces/ViewDocument?documentId=090140af805cfeee&_afrRedirect=22251219806445 75.

[e] Currently, Noxafil delayed-release tablets and oral suspension are indicated in patients 13 years of age and older and Noxafil injection is indicated in patients 18 years of age and older. The current efficacy supplement would expand use of Noxafil to children as young as 2 years of age.

	host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.			
		In addition to the indication above, oral suspension is indicated in patients 13 years of age and older for the treatment of oropharyngeal candidiasis (OPC)[f], including OPC refractory (rOPC) to itraconazole and/or fluconazole.		
Route of Administration	Oral	Oral	Oral	Intravenous infusion
Strength	300 mg per packet (30 mg/mL after mixing)	40 mg/mL	100 mg	300 mg/16.7 mL (18 mg/mL)
Dose and Frequency	For pediatric patients 2 to less than 18 years of age, for prophylaxis of invasive *Aspergillus* and *Candida* infections weighing less than or equal to 40 kg: 6 mg/kg twice daily on	200 mg (5 mL) three times a day. **OPC**: Loading dose: 100 mg (2.5 mL) twice a day on the first day. Maintenance dose: 100 mg (2.5 mL) once	Loading dose: 300 mg (three 100 mg delayed-release tablets) twice a day on the first day. Maintenance dose: 300 mg (three 100 mg delayed-release tablets) once a day, starting on	Loading dose: 300 mg Noxafil injection intravenously twice a day on the first day. Maintenance dose: 300 mg Noxafil injection intravenously once a day, starting on the second day.

[f] In addition to prophylaxis of invasive *Aspergillus* and *Candida* infections in the patients indicated.

	the first day and then 6 mg/kg once daily thereafter.	a day for 13 days. **rOPC**: 400 mg (10 mL) twice a day.	the second day.	
How Supplied	Package A: a kit with 8 child-resistant single-use packets of Noxafil for Delayed-Release Oral Suspension 300 mg, two 3 mL (green) notched tip syringes, two 10 mL (blue) notched tip syringes, two mixing cups, one mixing liquid bottle, and one bottle adapter for the mixing liquid bottle. Package B: a box of six 3 mL (green) and six 10 mL (blue) notched tip syringes.	4-ounce bottle containing 105 mL of suspension. Supplied with each oral suspension bottle is a plastic dosing spoon calibrated for measuring 2.5-mL and 5-mL doses.	Bottles of 60 delayed-release tablets	Carton containing one single-dose vial.
Storage	Store the entire kit at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) in a clean, dry place. Do not	Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room	Store at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].	Unreconstituted vial should be store refrigerated at 2-8°C (36-46°F).

	open foil packet containing the for delayed-release oral suspension until ready for use.	Temperature]. DO NOT FREEZE.		

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Noxafil PowderMix would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anti-Infectives (DAI) concurred with the findings of OPDP's assessment for Noxafil PowderMix.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

The proposed proprietary name, Noxafil, contains the United States Adopted Name (USAN) stem "-afil" in the suffix position of the name which is used by the USAN Council to indicate phosphodiesterase type 5 inhibitors (PDES) inhibitors.[g] Proprietary names should usually not incorporate USAN stems in the position that USAN designates for the stem.[h] The use of a USAN stem within proprietary names, even when used consistently with the USAN meaning, can result in multiple similar proprietary names and proprietary names that are similar to established names, thus increasing the chance of confusion among those drugs, which may compromise patient safety. To reduce the potential for confusion, USAN stems should usually not be incorporated into proprietary names.

However, the root name, "Noxafil", was initially approved in 2006 with the approval of Noxafil oral suspension, and subsequently with approval of Noxafil delayed-release tablets and injection, and these formulations are currently marketed. Additionally, our FDA Adverse Event Reporting System (FAERS) search completed in our previous review of the proposed proprietary name,

[g] USAN stem search conducted on February 26, 2021.

[h] Guidance for industry: Best practices in developing proprietary names for drugs. Draft Guidance May 2014. http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM39899.

Noxafil, under NDA 214770, yielded no cases describing name confusion.[i] Thus, based on the information considered above, in this case we do not object to the inclusion of the stem "-afil" in the proposed proprietary root name, Noxafil.

2.2.2 Components of the Proposed Proprietary Name

Merck indicated in their submission that the proposed proprietary name, "Noxafil PowderMix," includes "Noxafil," which is an FDA approved base brand name, and the modifier "PowderMix," which is "derived from Powder Mixture." We note that the root name, "Noxafil," does not contain any components (i.e. route of administration, dosage form, etc.) that are misleading or can contribute to medication error. However, we note that the proposed modifier, "PowderMix," begins with the letter string 'Po-.' 'PO,' is a medical abbreviation for the route of administration, by mouth, which may be used on a prescription to direct that the product is to be administered orally. In some circumstances, the incorporation of medical abbreviations in proprietary names can inadvertently be a source of error.[j] In this case, the proposed product is intended to be administered orally and thus is consistent with the meaning of the medical abbreviation 'po.' Although we typically discourage the inclusion of medical abbreviations in proprietary names, in this case, we do not object to the inclusion of the letter string 'Po-' in the prefix of the proposed modifier.

We note that the root name, "Noxafil," does not contain any components (i.e. route of administration, dosage form, etc.) that are misleading or can contribute to medication error. We discuss the use of the same root name, "Noxafil," for multiple dosage forms in Section 2.2.5 *Evaluation of the use of the same root name, "Noxafil," for Multiple Dosage Forms* and assess the modifier, "PowderMix," in Section 2.2.6 *Evaluation of the proposed modifier, "PowderMix."*

2.2.3 Comments from Other Review Disciplines at Initial Review

On February 26, 2021, the Division of Anti-Infectives (DAI) did not forward any comments or concerns relating to Noxafil PowderMix at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy-nine practitioners participated in DMEPA's prescription studies for Noxafil PowderMix. We note that 6 of the Rx simulation study participants (3 inpatient, 2 voice, and 1 outpatient) did not include the modifier "PowderMix" in their response. We further discuss the results of a dropped modifier in subsection 2.2.6, *Evaluation of the proposed modifier, "PowderMix."*

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.

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[i] Myers, D. Proprietary Name Review for Noxafil (NDA 214770). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 03. Panorama No. 2020-41831928.

[j] Guidance Document: Best Practices in Developing Proprietary Names for Human Prescription Drug Products; Guidance for Industry. 2020. Available from: https://www fda.gov/regulatory-information/search-fda-guidance-documents/best-practices-developing-proprietary-names-human-prescription-drug-products-guidance-industry.

Appendix B contains the results from the prescription simulation studies.

2.2.5 Evaluation of the use of the same root name, "Noxafil," for Multiple Dosage Forms

The root name, "Noxafil," is currently marketed as an Oral Suspension, 40 mg/mL, Delayed-release Tablet, 100 mg, and Injection, 300 mg/16.7 mL (18 mg/mL). Merck now proposes a "powder for delayed-release oral suspension" formulation, intended to be supplied as packets containing 300 mg of posaconazole powder, to be marketed under the same root name, Noxafil. Merck developed the proposed "for delayed-release oral suspension" dosage formulation as an age appropriate oral formulation for pediatric patients, allowing for weight based dosing, as well as to enhance bioavailability and overcome the exposure limitations of the current oral suspension dosage formulation. We considered the appropriateness of using the root name, Noxafil, for the "powder for delayed-release oral suspension" formulation proposed under NDA 214770, which would represent a brand name extension for this product line. We note that the Noxafil oral suspension, delayed-release tablet, and injection, and the proposed "powder for delayed-release oral suspension" formulation will share the same active ingredient (posaconazole) and the same indication (for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy). However, the products differ in some characteristics including dosage form (for delayed-release oral suspension vs. Oral Suspension, Delayed-release Tablets, and Injection), strength (300 mg packets of powder, to be reconstituted to a 30 mg/mL strength vs. 40 mg/mL, 100 mg, and 300 mg/16.7 mL (18 mg/mL), route of administration (oral vs. intravenous infusion), patient population (current efficiency supplement proposes to expand the use of Noxafil to children as young as 2 years of age vs. currently the Noxafil Oral Suspension and Delayed-release tablets are indicated in patients 13 years of age and older and Noxafil injection is indicated in patients18 years of age and older), and recommended dosage (for pediatric patients 2 to less than 18 years of age weighing less than or equal to 40 kg: 6 mg/kg twice daily on the first day followed by 6 mg/kg once daily vs. 200 mg (5 mL) three times a day for the oral suspension, 300 mg twice a day on the first day followed by 300 mg once a day, starting on the second day for the delayed-release tablets and injection). Additionally, the oral suspension dosage formulation has an indication for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole in patients ages 13 to less than 18 years of age, at the dosage for OPC of 100 mg (2.5 mL) twice a day on the first day followed by 100 mg (2.5 mL) once a day for 13 days and the dosage for rOPC is 400 mg (10 mL) twice a day.

To help us better understand the pharmacokinetic (PK) and pharmacodynamic (PD) properties of the for delayed oral suspension and the oral suspension formulations, we conferred with the Division of Clinical Pharmacology (DCPIV). DCPIV stated that the Applicant did not directly compare the relative bioavailability of the approved Noxafil Oral Suspension (OS) and the proposed posaconazole for delayed-release oral suspension (PFS) in any clinical studies. However, based on topline PK properties of both products, they would not be considered bioequivalent with the PFS having a higher bioavailability than the OS. Furthermore, Clinical confirmed the difference in PK/PD between the two formulations (OS and PFS) is clinically significant.

It is a common and accepted practice to have a product line with multiple dosage forms share a root name with an appropriate modifier to distinguish when needed. Despite the differences noted above, we believe the risk can be appropriately managed via labeling and the existence of a modifier (see section 2.2.6 below). Therefore, in this instance, we do not object to the proposed for delayed-release oral suspension formulation being marketed under the same proprietary root name, Noxafil.

2.2.6 Evaluation of the proposed modifier, "PowderMix"

Merck proposes the modifier, "PowderMix," for their proposed "powder for delayed-release oral suspension" formulation, stating that "PowderMix" is "derived from Powder Mixture" and that the proposed proprietary name, "Noxafil PowderMix," "differentiates from the approved Noxafil oral suspension." We considered that "PowderMix" is a descriptive modifier intended to convey information about the product's composition (dosage form) and to provide differentiation from the currently marketed Noxafil oral suspension. We find that using a modifier to differentiate this product from the currently marketed Noxafil products is an acceptable approach to signify that there is a difference.

As part of our evaluation of the modifier, we assessed whether the modifier, "PowderMix," is currently utilized. We searched our internal databases, Drugs@FDA, and the Institute for Safe Medication Practices' (ISMP) List of Products with Drug Name Suffixes[k] and found that the modifier, "PowderMix," does not currently exist in drug nomenclature.

As we were unable to identify that the modifier "PowderMix" has been previously used, we considered its use as a descriptive modifier intended to convey information about the product's composition (dosage form). First, we considered inclusion of the word "powder" that when used to indicate a dosage form is defined by FDA Data Standards Manual (DSM)[l] as "an intimate mixture of dry, finely divided drugs and/or other chemicals that may be intended for internal or external use." We find that the aforementioned definition of the word "powder" is consistent with the proposed dosage formulation. Second, we also considered inclusion of the word "mix" within the modifier "PowderMix." The word "mix" used as a transitive verb can be defined as "to combine or blend into one mass," "to combine with another," "to bring into close association," and "to form by mixing components."[m] We find that the aforementioned definition "to form by mixing components" of the word "mix" is consistent with the proposed dosage formulation. Thus, the definitions of these words appear to provide support of Merck's intention to communicate via the modifier, "PowderMix," to provide differentiation from the currently

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[k] ISMP's List of Products with Drug Name Suffixes [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2010. Available from: https://www.ismp.org/sites/default/files/attachments/2018-04/drugnamesuffixes.pdf.

[l] Link to DSM (monographs) Dosage Form: http://wayback.archive-it.org/7993/20171115111312/https://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071666.htm.

[m] Merriam-Webster. "mix". In Merriam-Webster.com dictionary. Retrieved 2021 MAR 31, available from: https://www.merriam-webster.com/dictionary/mix.

marketed Noxafil oral suspension and information about the product's composition (dosage form).

It is not uncommon to use modifiers to differentiate products with certain differences in product characteristics within a product line. However, we also note that omission and oversight of a modifier is cited in literature as a cause of medication error.[n] Postmarketing experience shows that the introduction of product line extensions results in medication errors if the modifier is omitted or overlooked and the product characteristics are similar or overlap. Additionally, as we previously noted in subsection 2.2.4, *FDA Name Simulation Studies*, six (3 inpatient, 2 voice, and 1 outpatient) of the seventy-nine Rx simulation study participants did not include the modifier "PowderMix" in their response. Therefore, we considered the risk of name confusion if the modifier is dropped or overlooked.

We note that each Noxafil dosage form would be marketed as a single strength. If included on the prescription, the difference in product strength, 30 mg/mL for Noxafil PowderMix following reconstitution versus 40 mg/mL for the currently marketed oral suspension strength, could help differentiate these two formulations. However, we also considered that in some cases, prescriptions for single strength products are written without a strength. Because three of the dosage forms share the same root proprietary name, Noxafil, the dosage form or strength would need to be included on a prescription. However, we note that the proposed "PowderMix" product (after mixing with the supplied diluent) results in an oral suspension which is the same final dosage form as the currently marketed oral suspension. Therefore, we specifically considered the risk of confusion if the modifier "PowderMix" is dropped or overlooked, and the prescription directions include "po" (medical abbreviation for the route of administration, by mouth) and "mL" implying an oral liquid. If Noxafil oral suspension is inadvertently dispensed in place of Noxafil PowderMix or vice versa, these two formulations are not bioequivalent. Thus, wrong formulation medication errors could result in differences in clinical efficacy.

We considered and evaluated the risks associated with potentially using a dual proprietary naming strategy for the proposed product. However, we note that there is a potential for concomitant therapy since postmarketing experience with other drug products has shown duplicate therapy leading to overdoses when an active ingredient is marketed under two or more names.[o] Furthermore, given these products will have different dosages and strengths, managing them under separate names may increase the likelihood for this type of error occurring. Additionally, we considered a previous postmarket review[p] of FDA Adverse Event Reporting System (FAERS) cases involving confusion between the Noxafil oral suspension and delayed-release tablet dosage forms, which included Noxafil wrong dose medication errors. That review led to a Drug Safety Communication[q] to caution about dosing errors when switching between

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[n] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

[o] The Institute for Safe Medication Practices. 2009 JAN 29. Revatio=Sildenafil=Viagra. ISMP Med Saf Alert Acute Care. 14(2):1-2.

[p] Sheppard, J. Postmarket Medication Error Memo for Noxafil (NDAs 022003, 022027, and 205053). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 DEC 16. RCM No.: 2014-2597-03.

[q] A link to the complete FDA DSC can be accessed at https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm479782.htm.

different oral formulations of Noxafil, as well as implementation of labeling statements noting that Noxafil delayed-release tablets and oral suspension are not interchangeable due to the differences in the dosing of each formulation. We note that labeling statements have been added to address this risk on the carton and container labels and within the prescribing information.

Based on the information above, we have determined that the risks associated with potential dropping or overlooking of the modifier can be further mitigated through labeling strategies. Labeling considerations for this product will be addressed under separate cover.

Thus, when all the aforementioned mitigations are considered in totality, we find the modifier, "PowderMix," acceptable in this case, when used in conjunction with the root name Noxafil.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anti-Infectives (DAI). At that time we also requested additional information or concerns that could inform our review. On April 30, 2021, the Division of Anti-Infectives (DAI) stated no additional concerns with the proposed proprietary name, Noxafil PowderMix.

3 CONCLUSION

The proposed proprietary name, Noxafil PowderMix, is acceptable.

If you have any questions or need clarifications, please contact Nicholas Miles, OSE project manager, at 301-796-7025.

3.1 COMMENTS TO MERCK SHARP & DOHME CORP., A SUBSIDIARY OF MERCK & CO., INC.

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

If any of the proposed product characteristics as stated in your submission, received on February 2, 2021 and amendment received on February 12, 2021 are altered prior to approval of the marketing application, the name must be resubmitted for review.

REFERENCES

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

   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. [r]

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

***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.

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. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

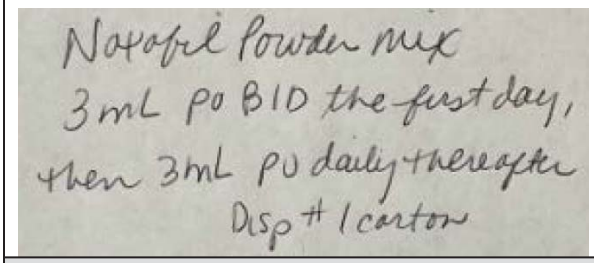
   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   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. Noxafil PowderMix Study (Conducted on March 5, 2021)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order: Noxafil Powder Mix give 180mg PO BID x1 then 180mg po once daily thereafter	Noxafil PowderMix Give 3 mL by mouth twice daily on the first day, then give 3 mL by mouth once daily thereafter Dispense 1 unit of use carton with 8 packets
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Noxafil PowderMix	

FDA Prescription Simulation Responses (Aggregate Report)

209 People Received Study
79 People Responded

Study Name: Noxafil PowderMix

Total	15	21	13	30	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
NAXABIL POWDER MIX	1	0	0	0	1
NAXAFRIL POWDER MIX	1	0	0	0	1
NOFAXIL POWDER MIX	0	0	0	1	1
NOSAFIL POWDER MIX	0	0	1	0	1
NOTOFIL POWDER MIX	2	0	0	0	2
NOXABIL POWDER MIX	1	0	0	0	1
NOXAFIL	1	0	1	3	5
NOXAFIL POWDER	0	0	0	6	6
NOXAFIL POWDER MIX	5	0	4	19	28
NOXAFIL POWDERMIX	0	21	0	0	21
NOXAFIL POWEDER MIX	0	0	0	1	1
NOXAFIL POWER MIX	0	0	1	0	1
NOXAPHIL POWDER MIX	0	0	2	0	2
NOXIFIL POWDER MIX	0	0	2	0	2
NOXIPHIL	0	0	1	0	1
NOXIVIL POWDER MIX	0	0	1	0	1
NOXOFIL POWDER	1	0	0	0	1
NOXOFIL POWDER MIX	2	0	0	0	2
NOXOFIL POWEDER	1	0	0	0	1

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/s/

DEBORAH E MYERS
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VALERIE S VAUGHAN
04/30/2021 12:05:50 PM

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:	November 3, 2020
Application Type and Number:	NDA 214770
Product Name and Strength:	Noxafil (posaconazole) powder for delayed-release oral suspension, 300 mg per packet (30 mg/mL, after mixing)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (Merck)
Panorama #:	2020-41831928
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Team Leader:	Otto L. Townsend, PharmD
DMEPA Deputy Director:	Irene Z. Chan, PharmD, BCPS

Contents

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

The proposed proprietary name, Noxafil, was approved with the approval of Noxafil Oral Suspension, 40 mg per mL (NDA 022003) on September 15, 2006. Subsequently, the proprietary name, Noxafil was approved for use with additional formulations: Noxafil Oral Suspension, 40 mg per mL (NDA 022027) approved October 20, 2006, Noxafil Delayed-release Tablets, 100 mg (NDA 205053) approved November 25, 2013, and Noxafil Injection, 300 mg/16.7 (18 mg/mL) (NDA 205596) approved September 13, 2014, and remains in use for such products.

On July 31, 2020, Merck submitted an efficacy supplement (S-012) to NDA 205596, to fulfill Postmarket Requirements (PMRs 2090-1 [NDA 205053] and 2132-1 [NDA 205596]). Under the PMRs, Merck was required to conduct a trial in patients, ages 2 to <18 years, to evaluate the pharmacokinetic, safety and tolerability of two new formulations of posaconazole (intravenous solution and/or new age appropriate oral formulation) in immunocompromised pediatric patients with known or expected neutropenia (PMRs 2090-2 [NDA 205053] and 2132-2 [NDA 205596]), and to conduct a comparative, double-blind, randomized, multi-center trial, in patients ages 2 to <18 years, to evaluate the safety, efficacy, and tolerability of posaconazole for prophylaxis of invasive fungal infections in pediatric patients with known or expected neutropenia. Thus, in this supplement, Merck proposes a new oral dosage formulation (powder for delayed-release oral suspension) for patients ages 2 to <18 years to support the pediatric indication for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy. Of note, this new formulation is not bioequivalent on a mg to mg basis with the currently marketed oral suspension formulations.

Subsequently, on August 3, 2020, Merck submitted the name, "Noxafil", as their proposed name for their proposed powder for delayed-release oral suspension formulation, under NDA 214770, in conjunction with their efficiency supplement that was submitted on July 31, 2020, under NDA 205596/S-012.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 3, 2020, that cross references supporting labeling documents submitted as part of the efficacy supplement to NDA 205596 on July 31, 2020.

Table 1. Relevant Product Information for Noxafil (NDAs 214770, 022003, 205053, and 205596)

	NDA 214770	NDA 022003	NDA 205053	NDA 205596
Approval Date	Not Applicable	09/15/2006	11/25/2013	03/13/2014

Intended Pronunciation	NOX-a-fil			
Active Ingredient	posaconazole			
Dosage Form	powder for delayed-release oral suspension	Oral Suspension	Delayed-release Tablets	Injection
Indication of Use[a]	In patients 2 years of age and older for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.			
		In addition to the indication above, oral suspension is indicated in patients 13 years of age and older for the treatment of oropharyngeal candidiasis (OPC)[b], including OPC refractory (rOPC) to itraconazole and/or fluconazole.		
Route of Administration	Oral	Oral	Oral	Intravenous infusion
Strength	300 mg per packet	40 mg/mL	100 mg	300 mg/16.7 mL (18 mg/mL)

[a] Currently, Noxafil delayed-release tablets and oral suspension are indicated in patients 13 years of age and older and Noxafil injection is indicated in patients 18 years of age and older. The current efficacy supplement would expand use of Noxafil to children as young as 2 years of age.

[b] In addition to prophylaxis of invasive *Aspergillus* and *Candida* infections in the patients indicated.

	(30 mg/mL after mixing)			
Dose and Frequency	For pediatric patients 2 to less than 18 years of age, for prophylaxis of invasive *Aspergillus* and *Candida* infections weighing less than or equal to 40 kg: 6 mg/kg twice daily on the first day and then 6 mg/kg once daily thereafter.	200 mg (5 mL) three times a day. **OPC**: Loading dose: 100 mg (2.5 mL) twice a day on the first day. Maintenance dose: 100 mg (2.5 mL) once a day for 13 days. **rOPC**: 400 mg (10 mL) twice a day.	Loading dose: 300 mg (three 100 mg delayed-release tablets) twice a day on the first day. Maintenance dose: 300 mg (three 100 mg delayed-release tablets) once a day, starting on the second day.	Loading dose: 300 mg Noxafil injection intravenously twice a day on the first day. Maintenance dose: 300 mg Noxafil injection intravenously once a day, starting on the second day.
How Supplied	Package A: a kit with 8 child-resistant single-use packets of Noxafil Powder for Delayed-Release Oral Suspension 300 mg, two 3 mL (green) notched tip syringes, two 10 mL (blue) notched tip syringes, two mixing cups, one mixing liquid bottle, and one bottle adapter for the mixing liquid bottle.	4-ounce bottle containing 105 mL of suspension. Supplied with each oral suspension bottle is a plastic dosing spoon calibrated for measuring 2.5-mL and 5-mL doses.	Bottles of 60 delayed-release tablets	Carton containing one single-dose vial.

	Package B: a box of six 3 mL (green) and six 10 mL (blue) notched tip syringes.			
Storage	Store the entire kit at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) in a clean, dry place. Do not open foil packet containing the powder for delayed-release oral suspension until ready for use.	Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. DO NOT FREEZE.	Store at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].	Unreconstituted vial should be store refrigerated at 2-8°C (36-46°F).

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Noxafil would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anti-Infectives (DAI) concurred with the findings of OPDP's assessment for Noxafil.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

The proposed proprietary name, Noxafil, contains the United States Adopted Name (USAN) stem "-afil" in the suffix position of the name which is used by the USAN Council to indicate

phosphodiesterase type 5 inhibitors (PDES) inhibitors.[c] Proprietary names should usually not incorporate USAN stems in the position that USAN designates for the stem.[d] The use of a USAN stem within proprietary names, even when used consistently with the USAN meaning, can result in multiple similar proprietary names and proprietary names that are similar to established names, thus increasing the chance of confusion among those drugs, which may compromise patient safety. To reduce the potential for confusion, USAN stems should usually not be incorporated into proprietary names.

However, the root name, "Noxafil", was initially approved in 2006 with the approval of Noxafil Oral Suspension, and subsequently with approval of Noxafil Delayed-release Tablets and Injection, and these formulations are currently marketed. Additionally, our FDA Adverse Event Reporting System (FAERS) search (see *Section 2.2.4*) yielded no cases describing name confusion. Thus, based on the information considered above, in this case we do not object to the inclusion of the stem "-afil" in the proposed proprietary name, Noxafil.

2.2.2 Components of the Proposed Proprietary Name

Merck indicated in their submission that the proposed proprietary name, Noxafil, is a "coined term with no intrinsic meaning." 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. We discuss the use of a single proprietary name for multiple dosage forms in Section 2.2.5.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, August 14, 2020 e-mail, the Division of Anti-Infectives (DAI) did not forward any comments or concerns relating to Noxafil at the initial phase of the review.

2.2.4 Medication Error Data Selection of Cases

On September 10, 2020, we searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A for a description of FAERS database) for name confusion errors involving Noxafil that would be relevant for this review.

Table 2. FAERS Search Strategy

FAERS Field	Search Terms
Initial FDA Receive Dates	FDA Rcvd Dates: September 15, 2006 (approval date for Noxafil) to September 10, 2020
Product Name	Noxafil
Verbatim Name	Noxafil

[c] USAN stem search conducted on September 9, 2020.

[d] Guidance for industry: Best practices in developing proprietary names for drugs. Draft Guidance May 2014. http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM39899

Product Active Ingredient	Posaconazole
Drug Role	Primary suspect
Event	DMEPA Official PNR Name Confusion Search Terms
Country (derived)	USA

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, we excluded the 8 retrieved reports because they did not describe name confusion.

2.2.5 Multiple Dosage Forms under a Single Proprietary Name

Noxafil is currently marketed as an Oral Suspension, 40 mg/mL, Delayed-release Tablets, 100 mg, and Injection, 300 mg/16.7 mL (18 mg/mL). Merck now proposes a "powder for delayed-release oral suspension" formulation, available as 300 mg packets of powder, to be reconstituted to a 30 mg/mL strength, to be marketed under the same name, Noxafil. Merck developed the proposed "powder for delayed-release oral suspension" dosage formulation as an age appropriate oral formulation for pediatric patients, allowing for weight based dosing, (b) (4) We considered the appropriateness of using the proprietary name, Noxafil, for the "powder for delayed-release oral suspension" formulation proposed under NDA 214770, which would represent a brand name extension for this product line. We note that the Noxafil Oral Suspension, Delayed-release Tablets, and Injection, and the proposed "powder for delayed-release oral suspension" formulation will share the same active ingredient (posaconazole) and an overlapping indication (for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy). However, the products differ in some characteristics including dosage form (powder for delayed-release oral suspension vs. Oral Suspension, Delayed-release Tablets, and Injection), strength (300 mg packets of powder, to be reconstituted to a 30 mg/mL strength vs. 40 mg/mL, 100 mg, and 300 mg/16.7 mL (18 mg/mL), route of administration (oral vs. intravenous infusion), patient population (current efficiency supplement proposes to expand the use of Noxafil to children as young as 2 years of age vs. currently the Noxafil Oral Suspension and Delayed-release tablets are indicated in patients 13 years of age and older and Noxafil injection is indicated in patients18 years of age and older), and recommended dosage (for pediatric patients 2 to less than 18 years of age weighing less than or equal to 40 kg: 6 mg/kg twice daily on the first day followed by 6 mg/kg once daily vs. 200 mg (5 mL) three times a day for the oral suspension, 300 mg twice a day on the first day followed by 300 mg once a day, starting on the second day for the delayed-release tablets and injection). Additionally, the oral suspension dosage formulation has an indication for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole in patients ages 13 to less than 18 years of age, at the dosage for OPC of 100

mg (2.5 mL) twice a day on the first day followed by 100 mg (2.5 mL) once a day for 13 days and the dosage for rOPC is 400 mg (10 mL) twice a day.

To help us better understand the pharmacokinetic (PK) and pharmacodynamic (PD) properties of the powder for delayed oral suspension and the oral suspension formulations, we conferred with the Division of Clinical Pharmacology (DCPIV). DCPIV stated that the Applicant did not directly compare the relative bioavailability of the approved Noxafil Oral Suspension and the proposed posaconazole powder for delayed-release oral suspension in any clinical studies. However, based on topline PK properties of both products, they would not be considered bioequivalent, with the delayed-release for oral suspension having a higher bioavailability than the oral suspension that is currently marketed. Furthermore, Clinical confirmed the significance of the difference in PK/PD between the two formulations is a difference in clinical efficacy.

We note that it is historically accepted practice for some products to have multiple dosage forms share one proprietary name, even when there are other differences in the dosage forms. However, when dosage formulations are not bioequivalent on a mg to mg basis, this has contributed to medication errors in the past. For example, with Noxafil we identified medication errors between the Noxafil tablet formulation, after it was introduced to market as the second Noxafil formulation, and the previously marketed Noxafil oral suspension. After approval of the Noxafil tablets, we began to receive reports of confusion between the delayed-release tablet and the oral suspension where the products were being interchanged one for another.[e] However, the delayed release tablets have a higher bioavailability when compared to the Noxafil oral suspension formulation. Therefore, in this instance, while we do not object to the proposed powder for delayed-release oral suspension formulation being marketed under the same proprietary root name, Noxafil, we have determined that additional measures need to be implemented to further minimize the risk for confusion between the formulations (see *Section 2.2.6*).

2.2.6 Evaluation of the Need for a Modifier

We evaluated whether or not, in this instance, the powder for delayed-release for oral suspension product requires a modifier to signal the delayed-release nature of the product and differentiate this dosage form from other Noxafil dosage forms, especially the currently marketed Noxafil oral suspension. We evaluated whether or not the lack of a modifier raises a potential safety concern, given the fact that the proposed powder for delayed-release for oral suspension product (after mixing with supplied mixing liquid) results in an oral suspension (30 mg/mL) which is the same final dosage formulation as the currently marketed oral suspension (40 mg/mL).

The powder for delayed-release for oral suspension and the currently marketed oral suspension have similar dosage forms (oral suspensions) that, as previously noted, are not bioequivalent with differences in clinical efficacy. These two formulations also have different strengths, patient populations, recommended dosages, and indications (see Table 3 below):

[e] Shepard, J. Label and Labeling Review Memorandum for Noxafil (NDAs 022003, 022027, 205053 and 205596). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 MAR 18. RCM No.: 2014-2587.

Table 3. Differences in Product Characteristics		
Dosage Formulation	**Proposed "powder for delayed-release oral suspension"**	**Marketed Noxafil Oral Suspension**
Strength	30 mg/mL	40 mg/mL
Patient population	2 years of age to less than 18 years of age and weighing less than or equal to 40 kg	13 years of age and older
Recommended dosage	for pediatric patients 2 to less than 18 years of age, for prophylaxis of invasive *Aspergillus* and *Candida* infections weighing less than or equal to 40 kg: 6 mg/kg twice daily on the first day followed by 6 mg/kg once daily	200 mg (5 mL) three times a day
		OPC: Loading dose: 100 mg (2.5 mL) twice a day on the first day. Maintenance dose: 100 mg (2.5 mL) once a day for 13 days.
		rOPC: 400 mg (10 mL) twice a day.
Indication	is only indicated for prophylaxis of invasive *Aspergillus* and *Candida* infections in children 2 years of age to less than 18 years of age weighing less than or equal to 40 kg)	oral suspension is the only Noxafil dosage formulation indicated for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole in patients ages 13 to less than 18 years of age

Based on these differences noted, we are concerned about potential medication errors, including wrong dosage form, wrong strength, and wrong dose, if the currently marketed Noxafil Oral Suspension and the proposed powder for delayed-release oral suspension were to be marketed under the root name, Noxafil, without an appropriate modifier to provide differentiation between them.

Modifiers can be used to convey distinguishing product characteristics or that a difference exists. For instance, a modifier in the proprietary name of a delayed-release product, such as this one, may help reduce the risk of the types of medication errors listed above. We recognize there are limitations to this approach since there is postmarketing evidence that modifiers have been omitted or overlooked; however, Noxafil is an antifungal, and improper dosing of this product can lead to serious adverse events. For example, a pediatric patient who requires the 30 mg/mL powder for delayed-release oral suspension product and receives the 40 mg/mL Noxafil Oral Suspension product would receive an underdose likely resulting in inadequate prophylaxis

against fungal infections. An alternative to using a modifier to distinguish the PFS product from the currently marketed Noxafil Oral Suspension and other Noxafil products is to use a different proprietary name (i.e. dual proprietary name). However, marketing the new product under a unique proprietary name also carries risk of medication errors, such as therapeutic duplication and overdoses.

Given the totality of the factors considered above, we believe the addition of a modifier, to the root name, Noxafil, could add an incremental measure of safety by communicating that the proposed drug is not the same as the currently marketed Noxafil Oral Suspension or other Noxafil dosage forms.

On October 30, 2020, we held a teleconference with Merck to discuss our preliminary findings regarding the proposed proprietary name, Noxafil, and our concerns regarding the lack of a modifier. We recommended a modifier be added to reduce risk of confusion between the currently marketed Noxafil Oral Suspension and the proposed powder for delayed-release oral suspension product, and Merck expressed understanding regarding the FDA's concerns. They indicated that they agreed with the idea of adding a modifier and had proposed one prior to the teleconference. Therefore, we also discussed Merck's email proposal (dated October 29, 2020) to add "(b) (4)" as a modifier to the root name, Noxafil, powder for delayed-release oral suspension product. We shared preliminary concerns that the use of "(b) (4)" as a modifier may not be sufficient to provide differentiation as both products (b) (4) and have similar dosage forms (oral suspensions) that are not bioequivalent with differences in clinical efficacy. Additionally, we noted that if the current efficiency supplement (NDA 205596/S-012) were to be approved, both the currently marketed Oral Suspension, as well as proposed Powder for Delayed-Release Oral Suspension would be indicated for use for children as young as age 2. Therefore, we recommended that Merck consider developing another modifier to help to prevent medication errors (e.g., wrong dosage form, wrong strength, and wrong dose). FDA emphasized that the goal is to develop a modifier that can minimize the risk of the products being confused or inadvertently substituted for one another. Merck expressed understanding regarding the concerns stated about using "(b) (4)" as a modifier, and they stated that they intend to develop an appropriate modifier for use with the root name that will be submitted following receipt of our Noxafil (NDA 214770) Proprietary Name Request – decision letter.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anti-Infectives (DAI) via e-mail on October 30, 2020. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anti-Infectives (DAI) on November 3, 2020, they stated no additional concerns with the proposed proprietary name, Noxafil.

3 CONCLUSION

The proposed proprietary name, Noxafil, is not acceptable from a safety perspective. The proposed proprietary name, Noxafil, is vulnerable to name confusion because the proposed proprietary name does not distinguish this delayed-release product formulation from other currently marketed Noxafil drug formulations, including the currently marketed Oral Suspension

product formulation. Therefore, the decision to deny the name will be communicated to Merck via letter (See Section 3.1).

If you have further questions or need clarifications, please contact Nicholas Miles, OSE project manager, at 301-796-7025.

3.1 COMMENTS TO MERCK SHARP & DOHME CORP., A SUBSIDIARY OF MERCK & CO., INC.

We have completed our review of the proposed proprietary name, Noxafil, and have concluded that this name is unacceptable for the following reason:

The proposed proprietary name, Noxafil, is vulnerable to name confusion because the proposed proprietary name does not distinguish this delayed-release product formulation from other currently marketed Noxafil drug formulations, including the currently marketed Oral Suspension product formulation. We note that your proposed Noxafil powder for delayed-release oral suspension and your currently marketed Oral Suspension are not bioequivalent and cannot be substituted one for the other on a mg per mg basis, which may lead to medication errors with potentially significant clinical impact. We are concerned about potential medication errors, including wrong dosage form, wrong strength, and wrong dose, if the proposed powder for delayed-release oral suspension were to be marketed under the root name, Noxafil, without an appropriate modifier to provide differentiation from other Noxafil formulations. Our safety analysis indicates that the use of an appropriate modifier with your proposed proprietary name may help distinguish this delayed-release product formulation from other drug formulations within the Noxafil product line, including your currently marketed Oral Suspension product formulation.

During our October 30, 2020, teleconference, we shared our preliminary findings regarding the proposed proprietary name, Noxafil. We expressed concerns regarding the lack of a modifier, as well as concerns we identified with your emailed proposal to use "(b) (4)" as the modifier. During this teleconference we recommended a modifier be added that can minimize the risk of the products being confused or inadvertently substituted for one another, and you expressed understanding regarding our concerns. You indicated that you agreed with adding a modifier and that you intend to develop an appropriate modifier for use with the root name, Noxafil.

For additional information, we refer you to our Draft Guidance, Best Practices in Developing Proprietary Names For Drugs (May 2014)[f] where we provide some additional guidance regarding modifiers.

We recommend that you submit a new request for a proprietary name review for Noxafil, in which you include an appropriate modifier as part of your proposed proprietary name.

[f] When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

APPENDIX A: 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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