CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219104Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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 7, 2024
Application Type and Number:	NDA 219104
Product Name, Dosage Form, and Strength:	Prevymis (letermovir) Oral Pellets, 20 mg and 120 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Merck Sharp & Dohme Corp (Merck)
PNR ID #:	2024-1044725825
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph.
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1 INTRODUCTION

This review evaluates the proposed proprietary name, Prevymis, 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

Prevymis (letermovir) tablet and injection were approved on November 8, 2017 under NDA 209939 and NDA 209940 for the prophylaxis of cytomegalovirus (CMV) infection and disease in adult patients.

Merck is pursuing a pediatric indication and an oral pellet formulation in patients weighing (b) (4) (b) (4) therefore, submitted the name, Prevymis, for review under NDA 219104 on June 4, 2024.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on June 4, 2024[a].

Table 1. Relevant product information for Prevymis oral pellets and Prevymis tablet and injection[b]

	Prevymis (Proposed Oral Pellets)	Prevymis
Initial Approval Date	N/A	November 8, 2017
Intended Pronunciation	PREH vih miss	
Active Ingredient	letermovir	
Indication	-Prophylaxis of cytomegalovirus (CMV) infection and disease in adult and pediatric CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). (1.1) -Prophylaxis of CMV disease in adult and pediatric kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-])	

[a] Request for Proprietary Name Review (NDA 219104; Prevymis). Rahway (NJ): Merck Sharp & Dohme Corp; 2024 June 4. Available from: \\CDSESUB1\evsprod\NDA219104\0012\m1\us.

[b] New Drug Application (NDA 219104; Prevymis). Rahway (NJ): Merck Sharp & Dohme Corp; 2024 Mar 1. Available from:\\CDSESUB1\evsprod\NDA219104\0001\m1\us.

	Pediatric indication also under review in NDA 209939/S-013& NDA 209940/S-012	
Route of Administration	Oral	Oral; Intravenous
Dosage Form	Oral pellets	Oral tablets; Injection
Strength	20 mg and 120 mg per packet	Tablets: 240 mg and 480 mg Injection: 240 mg/12 mL (20 mg/mL) and 480 mg/24 mL (20 mg/mL)
Dose and Frequency	Recommended Dosage for Adult and Pediatric Patients 12 Years of Age and Older: 480 mg orally or intravenously once daily. Initiate Prevymis between Day 0 and Day 28 post-transplantation (HSCT) or Day 0 to Day 7 (kidney transplant). Continue through day 100 post-HSCT and day 200 in post-HSCT patients at risk for late CMV and kidney transplant. If PREVYMIS is co-administered with cyclosporine, the dosage of PREVYMIS should be decreased to 240 mg once daily in adult and pediatric patients 12 years of age and older. Recommended of Pediatric Patients Less than 12 Years of Age (proposed pellet NDA 219104) and injection (b) (4)	

	(b) (4)	
18 k		
7.5		
5 kg		
2.5		
How Supplied	Packets containing 20 mg or 120 mg of Prevymis oral pellets packaged into a carton. Each carton contains 30 child resistant packets.	Cartons contain 240 mg or 480 mg tablets -Cartons containing four dosepaks, each dosepak contains a 7-count blister card for a total of 28 tablets -Cartons containing two unit-dose 7-count blister cards for a total of 14 tablets Injection: -Single-dose vials containing 240 mg/12 mL or 480 mg/24 mL of Prevymis
Storage	Store PREVYMIS oral pellets in the original packet until use. Store PREVYMIS oral pellets at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].	Tablets: Store PREVYMIS tablets in the original package until use. Store PREVYMIS tablets at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Injection:

		Store PREVYMIS injection vials at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store in the original carton to protect from exposure to light.

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Prevymis would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Prevymis. The Division of Antivirals (DAV) concurred with the findings of OPDP's assessment for Prevymis.

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Merck did not provide a derivation or intended meaning for the proposed proprietary name, Prevymis, 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 can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

On June 18, 2024, the Division of Antivirals (DAV) did not forward any comments or concerns relating to Prevymis at the initial phase of the review.

2.2.4 SAFETY ASSESSMENT OF THE PROPOSED NAME, PREVYMIS

Merck is proposing a new dosage form, oral pellets as a product line extension. The proposed formulation shares the same active ingredients (letermovir) as the approved Prevymis products but differ in strength [Pellets: 20 mg and 120 mg versus Tablets: 240 mg and 480 mg; Injection:

[c] USAN stem search conducted on October 27, 2024.

240 mg/12 mL (20 mg/mL) and 480 mg/24 mL (20 mg/mL)]. The oral pellet is being developed to provide for oral pediatric dosing and for dosing patients unable to swallow tablets. Proposed dosing recommendations can be achieved using either the oral tablet or oral pellets (see Table 1 above). Further, feedback from the clinical pharmacology reviewer has determined that the oral pellets and tablet dosage forms are equivalent on a milligram-per-milligram basis [240mg (2 x120 mg) oral pellets demonstrated comparable relative bioavailability with 240 mg tablet].

We considered whether these products sharing the same proprietary name, Prevymis, may lead to medication errors. However, since the dosage forms (tablet and pellets) are equivalent, we determined that label and labeling mitigations may adequately address any residual risk of product confusion.

Furthermore, we note that through our routine monitoring we have not identified any medication errors involving name confusion with the proprietary name Prevymis. Therefore, given the precedence for using this naming convention, and the absence of any medication errors involving the proprietary name, we find the Sponsor's proposal to market the proposed product with the proprietary name Prevymis acceptable. It is a common and accepted practice to have multiple dosage forms of an active ingredient managed under one proprietary name (e.g., Renvela and Pradaxa). Given the dosage forms are equivalent, we determined that label and labeling mitigations may adequately address any residual risk of product confusion. In this specific case, we have determined that the different dosage forms and strengths can be managed under a single proprietary name. Therefore, we do not have concerns with the use of Prevymis as the proprietary name for the proposed oral pellet formulation.

2.2.5 COMMUNICATION OF DMEPA'S DETERMINATION

On August 7, 2024, DMEPA 1 communicated our determination to the Division of Antivirals (DAV).

3 CONCLUSION

The proposed proprietary name, Prevymis, is conditionally acceptable.

3.1 COMMENTS TO MERCK SHARP & DOHME CORP

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

If any of the proposed product characteristics as stated in your submission, received on June 4, 2024, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. United States Adopted Names (USAN) Stems

USAN Stems List contains all the recognized USAN stems, available at https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems.

5 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, the Office of Prescription Drug Promotion (OPDP) assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by the Office of Non-Prescription Drugs (ONPD). OPDP or ONPD 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 ONPD 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 3*. 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.[d]

*Table 3. 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?

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

*Table 3. 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.	
	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. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, Cerner RxNorm, Purple Book, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 4-6) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 4).

- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[e]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 5).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA also conducts 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

[e] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND), Office of Generic Drugs (OGD), and/or Office of Pharmaceutical Quality (OPQ) for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the Safety Evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

   Additionally, other review disciplines opinions such as OPQ 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 Safety Evaluator 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.

Table 4. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.

Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?

Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤69%).**		
Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg	
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.	
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? • Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤69%).**		
	• Are the lengths of the names dissimilar* when scripted? • *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	• Across a range of dialects, are the names consistently pronounced differently?

Table 6. Low Similarity Name Pair Checklist (i.e., combined score is **≤54%).**
Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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