CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215110Orig1s000

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:	March 8, 2021
Application Type and Number:	NDA 215110
Product Name and Strength:	Mavyret (glecaprevir and pibrentasvir) oral pellets, 50 mg/20 mg
Product Type:	Multiple Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	AbbVie, Inc.
Panorama #:	2020-44282956
DMEPA Safety Evaluator:	Melina Fanari, RPh
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Mavyret, 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. AbbVie, Inc. did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Mavyret (glecaprevir and pibrentasvir) tablet was approved on August 3, 2017 under NDA 209394 for the treatment of chronic hepatitis C virus in adults (b) (4)

AbbVie, Inc. is pursuing a oral pellet formulation in patients 3 years and older, therefore submitted the name, Mavyret, for review under NDA 215110 on December 10, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on December 10, 2020.

Table 1. Relevant product information for Mavyret Pellets and Mavyret tablet[a]

	Mavyret Pellets	Mavyret tablet
Initial Approval Date	N/A	August 3, 2017
Intended Pronunciation	not provided	
Active Ingredient	Glecaprevir and pibrentasvir	
Indication	1) indicated for the treatment of adult and pediatric patients 3 years and older (b) (4) with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A), 2) indicated for the treatment of adult and pediatric patients 3 years and older (b) (4) with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.	(b) (4)

[a] Mavyret Product information obtained at https://dailymed nlm nih.gov/dailymed/lookup.cfm?setid=7bf99777-0401-9095-8645-16c6e907fcc0, Accessed January 11, 2021.

<table>
<tr><td>Route of Administration</td><td colspan="2">Oral</td></tr>
<tr><td>Dosage Form</td><td>Oral pellets</td><td>Oral tablets</td></tr>
<tr><td>Strength</td><td>glecaprevir 50 mg / pibrentasvir 20 mg</td><td>glecaprevir 100 mg / pibrentasvir 40 mg</td></tr>
<tr><td>Dose and Frequency</td><td>Dose and Frequency: The number of packets and dosage based on body weight for pediatric patients 3 years (b) (4) (weighing (b) (4) less than 45 kg) are shown in table below:
<table>
<tr><th>Body Weight (kg)</th><th>Number of MAVYRET Oral Pellets in Packets</th><th>Daily Dose of glecaprevir/pibrentasvir</th></tr>
<tr><td>(b) (4) < 20 kg</td><td>Three 50 mg/20 mg packets of pellets once daily</td><td>150 mg/60 mg per day</td></tr>
<tr><td>(b) (4) 20 to < 30 kg</td><td>Four 50 mg/20 mg packets of pellets once daily</td><td>200 mg/80 mg per day</td></tr>
<tr><td>(b) (4) 30 to < 45 kg</td><td>Five 50 mg/20 mg packets of pellets once daily</td><td>250 mg/100 mg per day</td></tr>
</table></td><td>Recommended Dosage in Adult (b) (4)
3 tablets taken at the same time once daily or glecaprevir 300 mg and pibrentasvir 120 mg
Duration of the treatment varies from 8 -16 weeks as it based on the patient population in HCV mono-infected and HCV/HIV-1 co-infected patients with compensated liver disease (with or without cirrhosis) and with or without renal impairment including patients receiving dialysis.</td></tr>
<tr><td>How Supplied</td><td>Unit dose packets in cartons. Each carton contains 60 packets.</td><td>• 4-Week Carton
• 8-Week Carton (b) (4)</td></tr>
<tr><td>Storage</td><td colspan="2">Store at or below 30°C (86°F)</td></tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

AbbVie, Inc. did not provide a derivation or intended meaning for the proposed proprietary name, Mavyret, 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, Janaury 15, 2021 e-mail, the Division of Antivirals (DAV) did not forward any comments or concerns relating to Mavyret at the initial phase of the review.

2.2.4 Medication Error Data Selection of Cases

On January 8, 2021, 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 ***Mavyret*** that would be relevant for this review.

Table 2. FAERS Search Strategy

FAERS Field	Mavyret
Initial FDA Receive Dates	August 3, 2017 – January 8, 2010
Product Name	Mavyret
Verbatim Name(s)	n/a
Product Active Ingredient	Glecaprevir\pibrentasvir
Drug Role	n/a
Event	Medication errors(narrow)
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, 0 relevent reports related to name confusion with Mavyret were retrieved.

[b] USAN stem search conducted on November 30, 2020.

2.2.5 Safety Assessment of the Proposed Name, Mavyret

The Applicant proposes a new dosage form, oral pellets (50 mg glecaprevir and 20 mg pibrentasvir per packet), as a product line extension. The proposed formulation shares the same active ingredients as the approved Mavyret product (100 mg glecaprevir and 40 mg pibrentasvir per tablet), but differ in strength. We considered whether these products sharing the same proprietary name, Mavyret, may lead to confusion.

We note that Mavyret pellet and tablet differ in strength (50 mg/20 mg per packet vs 100 mg/40 mg per tablet) and dose (see table 1 above). Based on the information contained within the NDA submission, we note that the oral pellet formulation is not bioequivalent on a mg-to-mg basis with the currently marketed tablet formulation. Further, we note that the tablet and oral pellet formulations are both single strength products (100 mg/40 mg versus 50 mg/20 mg) and doses for the different indications are achievable given the proposed strengths. Therefore, a prescription could be written or ordered for the tablet formulation, but a patient dispensed the oral pellet formulation, or vice versa. For example, "Mavyret 300 mg/120 mg once daily" (intended tablet formulation) could be dispensed as "Mavyret oral pellets 6 packets daily" and lead to administration of the wrong formulation. Alternatively, "Mavyret 200 mg/80 mg once daily" (intended oral pellet formulation) could be dispensed as "Mayyret 2 tablets once daily" and also lead to the administration of the wrong formulation.

DMEPA shared the above concerns in an information request (IR) dated February 26, 2021 to the sponsor and requested that Abbvie describe the clinical consequences of medication errors associated with inadvertent formulation substitution and provide plans to mitigate such errors. In response to the Agency's IR, Abbvie stated that "*while the oral pellet formulation is not bioequivalent on a mg-to-mg basis to the currently marketed tablet formulation, the difference of [glecaprevir and pibrentasvir] exposures between the two formulations are not expected to be clinically significant or to impact the efficacy and safety outcomes of the patients*." Furthermore, *"If pediatric patients can swallow Mavyret tablets, based on the exposure difference between the pellets and tablets as well as the 300 mg/120 mg vs. 200 mg/80mg doses, the exposures of Mavyret tablets in this pediatric population are expected to fall within the efficacious and safe concentration range that has been established. Therefore, although there is no existing data in this scenario to assess the impact on drug efficacy and safety when Mavyret tablets are administered to this pediatric population, minimal efficacy or safety concerns are expected in this patient population."* Abbvie's response was also confirmed by the clinical review team in DAV, who stated that there are no efficacy or safety concerns if the formulations were interchanged during dispensing. Abbvie also provided their plan for product packaging differentiation and labeling statements to mitigate the residual risk.

Based on the totality of the information provided, we find the response to the IR adequate and determined that label and labeling mitigations can adequately address any risk of product confusion as described above. Our review of product labeling and packaging will be conducted under separate cover. Therefore, in this case, we find that the multiple formulations/dosage forms and strengths can be managed under one proprietary name and we do not have concerns with extending the use of Mavyret as a proprietary name for the oral pellet formulation.

3 CONCLUSION

The proposed proprietary name, Mavyret, is acceptable.

If you have any questions or need clarifications, please contact Mammah Borbor, OSE project manager, at 301-796-7731.

3.1 COMMENTS TO ABBVIE, INC.

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

If any of the proposed product characteristics as stated in your submission, received on December 10, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

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.

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. [c]

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

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. 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, CernerRxNorm, 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 3-5) 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 3).
- 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[d]. 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 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) 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.

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

c. 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.

d. 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.

Table 3. 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 4: 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. • 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?	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? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: 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.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MELINA N FANARI
03/08/2021 11:58:03 AM

SEVAN H KOLEJIAN
03/08/2021 11:58:03 AM