CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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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 26, 2015
Application Type and Number:	NDA 204370
Product Name and Strength:	Vraylar (cariprazine) Capsules 1.5 mg, 3 mg, 4.5 mg, and 6 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Forest Laboratories, Inc.
Panorama #:	2015-48257 and 2015-48262
DMEPA Primary Reviewer:	Deborah Myers, RPh, MBA
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1 INTRODUCTION

This review evaluates the proposed proprietary name, Vraylar, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by (b) (4), for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, Vraylar on January 17, 2013. The Division of Medication Error Prevention and Analysis (DMEPA) found the name, Vraylar, conditionally acceptable in OSE Review #2013-287, dated April 16, 2013.

Due to the amount of time that has passed since this conditional approval, the Applicant resubmitted the name, Vraylar, for review on January 22, 2015, to reassess for potential conflicts.

We note that since the initial NDA submission, the Applicant has (b) (4) .

1.2 PRODUCT INFORMATION

The following product information is provided in the January 22, 2015 proprietary name submission.

- Intended Pronunciation: VRAY-lar
- Active Ingredient: cariprazine; cariprazine is a new molecular entity (NME)
- Indication of Use: acute treatment of manic or mixed episodes associated with bipolar I disorder and treatment of schizophrenia
- Route of Administration: oral
- Dosage Form: capsule
- Strength: 1.5 mg, 3 mg, 4.5 mg, and 6 mg
- Dose and Frequency: once daily with or without food
- How Supplied: all strengths are supplied as a 30-count bottle, 90-count bottle, and 100-count box (hospital unit dose); 7-count blister packs in two configurations: 7 x 1.5 mg capsules and 1 x 1.5 mg plus 6 x 3.0 mg
- Storage: Store at 25°C (77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) *[see USP Controlled Room Temperature]*. Protect 3 mg and 4.5 mg capsules from light to prevent potential color fading.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Division of Psychiatry Products (DPP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Vraylar, 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 FDA Name Simulation Studies

103 practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, February 26, 2015 e-mail, the Division of Psychiatry Products (DPP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from the external name study conducted by (b) (4).

[1]USAN stem search conducted on February 5, 2015.

[2]POCA search conducted on February 6, 2015.

Table 1. POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	66
Low similarity name pair: combined match percentage score ≤49%	16

2.2.6 Names with Potential Orthographic, Spelling, and Phonetic Similarities that overlap in strength

The proposed product, Vraylar will be available in strengths of 1.5 mg, 3 mg, 4.5 mg, and 6 mg. Since these are not typical or commonly marketed strengths, we searched the Pragmatic® Regulated Product Labeling Listing and Registration System (PR°PLLR™) database to identify any names with potential orthographic, spelling, and phonetic similarities with Vraylar that were not identified in POCA, and found to have an overlap in strength with Vraylar.

Table 1A. (PR°PLLR™) Search Results	POCA score
No names identified.	N/A

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 83 names contained in Table 1 determined all 83 names will not pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Division of Psychiatry Products (DPP) via e-mail on March 23, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DPP on March 25, 2015, they stated no additional concerns with the proposed proprietary name, Vraylar.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have further questions or need clarifications, please contact Vasantha Ayalasomayajula, OSE project manager, at 240-402-5035.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your January 22, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE 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 DNCE 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. [3]

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. 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 50% 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 ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤49%.

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 with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it 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, etc.) may be limited when the strength or dose overlaps. We review 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.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

   Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

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 do 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 ≥50% 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: o 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. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o 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 ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Vraylar Study (Conducted on February 18, 2015)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Vraylar	Vraylar 1.5 mg, 1 capsule once daily with food, Dispense #30
Outpatient Prescription:	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

			251 People Received Study 103 People Responded
Study Name: Vraylar			
Total	**33**	**34**	**36**

INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
FRALAR	0	3	0	3
FRAYLAR	0	1	0	1
FREILAR	0	1	0	1
FRELAR	0	3	0	3
PRELAR	0	2	0	2
PREYLAR	0	1	0	1
RAYLAR	0	3	0	3
RELARD	0	1	0	1
REYLAR	0	1	0	1
URAYLAL	1	0	0	1
URAYLAR	3	0	0	3
VAYLAC	1	0	0	1
VAYLAR	0	1	0	1
VLAYCAR	0	0	2	2
VRACAR	0	0	1	1
VRAELAR	0	1	0	1
VRAGCAR	0	0	1	1
VRAGLAR	1	0	0	1
VRAILAR	0	1	0	1
VRALAR	0	3	1	4
VRAYCAR	0	0	19	19
VRAYLAC	2	0	0	2
VRAYLAE	4	0	0	4
VRAYLAI	3	0	0	3
VRAYLAR	18	6	11	35
VREILLAR	0	1	0	1
VRELAR	0	3	0	3
VREMAR	0	1	0	1
VREYLAR	0	1	0	1
VSAYCAR	0	0	1	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Vraylar **Established name:** cariprazine **Dosage form:** capsule **Strength(s):** 1.5 mg, 3 mg, 4.5 mg, and 6 mg **Usual Dose:** once daily with or without food	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Vraylar	100	Name is the subject of this review.

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Remular	59
2.	Synalar	56
3.	Valstar	55
4.	Viril Lam	52
5.	Viadur	51

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Vraylar **Established name:** cariprazine **Dosage form:** capsule **Strength(s):** 1.5 mg, 3 mg, 4.5 mg, and 6 mg **Usual Dose:** once daily with or without food	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Thyrolar	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and Thyrolar contains an extra syllable.
2.	Thyrolar-0.25	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and the root name Thyrolar contains an extra syllable.
3.	Thyrolar-0.5	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and the root name Thyrolar contains an extra syllable.
4.	Thyrolar-1	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and the root name Thyrolar contains an extra syllable.
5.	Thyrolar-2	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and the root name Thyrolar contains an extra syllable.
6.	Thyrolar-3	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and the root name Thyrolar contains an extra syllable.
7.	Thyrolar-5	58	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different, and

			the root name Thyrolar contains an extra syllable.
8.	Verelan	56	The infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Verelan name contains an extra syllable.
9.	Valchor	54	The infixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different.
10.	Virasal	53	The infixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Virasal contains an extra syllable.
11.	Basaglar	52	The prefixes of this name pair have sufficient orthographic differences. The second syllable of this name pair sound different, and Basaglar contains an extra syllable.
12.	(b) (4)***	52	The infixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and (b) (4) contains an extra syllable.
13.	Vorapaxar	52	The infixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Vorapaxar contains two extra syllables.
14.	(b) (4)***	51	The infixes and suffixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and the root name (b) (4) contains an extra syllable.
15.	Zyclara	51	The prefixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different, and Zyclara contains an extra syllable.
16.	Tafinlar	50	The prefixes and infixes of this name pair have sufficient orthographic differences. The first syllable of this name pair sound different, and Tafinlar contains an extra syllable.

17.	Zemplar	50	The prefixes of this name pair have sufficient orthographic differences. The first syllables of this name pair sound different.
18.	Versiclear	50	The infixes of this name pair have sufficient orthographic differences. The second syllable of this name pair sound different, and Versiclear contains an extra syllable.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Sular	48
2.	Cefaclor	44
3.	Valacyclovir	44
4.	Zymar	42
5.	Reglan	42
6.	Viagra	40
7.	Verapamil	38
8.	Valium	36
9.	Skyla	36
10.	Valtrex	34
11.	Varenicline	33
12.	Valcyte	32
13.	Vytorin	32
14.	Vyvanase	32
15.	Viibryd	30
16.	Uroxatral	24

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Vetalar	68	Veterinary product in Great Britain and Ireland
2.	Proklar	62	Discontinued per Drugs@FDA; ANDA 080273 Withdrawn FR Effective 3/23/1993, no generic available
3.	Dialar	59	International product marketed in UK by Sandoz
4.	Synalar 1:10	56	International product manufactured by Derma UK
5.	Synalar 1:4	56	International product manufactured by Derma UK
6.	Valclair	56	International product, formerly marketed in the UK and discontinued October 2008
7.	Veracur	53	International product per Martindale (Typharm, Ireland)
8.	Virovir	52	International product, marketed in India
9.	Doxylar	50	International product marketed in UK by Sandoz
10.	Vital-Chlor	50	OTC Animal drug
11.	Vivalan	50	International product - Discontinued and no longer actively marketed; approved in Italy, Belgium, England, Ireland, Germany, Portugal, Spain, the former Yugoslavia, France, and Slovakia

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Tracleer	62
2.	Curaler	60
3.	Flagyl ER	60
4.	Duraflor	58
5.	Zerlor	58
6.	Dri-Ear	56
7.	Firazyr	56
8.	Furalan	56
9.	Oralair 100	56
10.	Oralair 300	56
11.	(b) (4) ***	56
12.	Zaclir	56
13.	Qdall AR	56
14.	Raniclor	54
15.	Ablavar	53
16.	Dralserp	52
17.	Drize-R	52
18.	Fluralaner	52
19.	Formalaz	52
20.	Pro Clear	52
21.	Ramodar	52
22.	Raxar	52
23.	Tri-Chlor	52
24.	Trelstar	51
25.	Zelapar	51
26.	Bretylol	50
27.	Parathar	50

28.	Prevnar	50
29.	Prevnar 13	50
30.	Relera	50
31.	Resflor	50
32.	Trasylol	50

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/s/

DEBORAH E MYERS
03/26/2015

DANIELLE M HARRIS
03/26/2015

IRENE Z CHAN
03/26/2015

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	April 16, 2013
Reviewer(s):	Loretta Holmes, BSN, PharmD Division of Medication Error Prevention and Analysis
Team Leader:	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director:	Carol A. Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Vraylar (Cariprazine Hydrochloride) Capsules 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)
Application Type/Number:	NDA 204370
Applicant:	Forest Laboratories, Inc.
OSE RCM #:	2013-287

***** This document contains proprietary and confidential information that should not be released to the public.*****

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Vraylar, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 PRODUCT INFORMATION

The following product information was provided in the January 17, 2013 proprietary name submission.

- Active Ingredient: Cariprazine Hydrochloride; Cariprazine is a New Molecular Entity (NME)
- Indication of Use: Treatment of schizophrenia; Acute treatment of manic or mixed episodes associated with bipolar I disorder
- Route of Administration: Oral
- Dosage Form: Capsules
- Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)
- Dose and Frequency of Administration:
  - *Schizophrenia*
    The recommended dose range is (b) (4) once daily. Should be administered starting with 1.5 mg on Day 1 and increased to 3 mg on Day 2. Depending upon clinical response and tolerability, dose adjustments can be made upward or downward in 1.5 mg or 3 mg increments.
  - *Manic or Mixed Episodes Associated with Bipolar I Disorder*
    The recommended dose range is (b) (4) once daily. Should be administered starting with 1.5 mg on Day 1 and increased to 3 mg on Day 2. Depending upon clinical response and tolerability, dose adjustments can be made upward or downward in 1.5 mg or 3 mg increments.
- How Supplied:
  - 30-count and 90-count bottles
  - Hospital Unit Dose (10 x 10-count blister cards)
  - (b) (4)
  - Professional sample cartons containing one 7-count blister
- Storage: Store at 25°C (77°F); excursions permitted to 15°C and 30°C (to 59°F and 86°F)
- Container and Closure Systems: HDPE bottles have (b) (4) caps; the blister pack descriptions do not state whether or not they are child resistant

- Intended Pronunciation of the Proposed Proprietary: VRAY-lar
- Derivation of the Proposed Proprietary Name: Not derived from any particular concept

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Psychiatry Products (DPP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The February 25, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Vraylar, is not derived from any particular concept. 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.

2.2.4 FDA Name Simulation Studies

Ninety-three practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with currently marketed products nor did they appear or sound similar to any currently marketed products or products pending approval. Nine of the 28 participants in the verbal study interpreted the first letter "V" as the letter "F" and three participants in the same study omitted the first letter "V" and interpreted the name as starting with "R". See Appendix C for the complete listing of interpretations from the verbal and written prescription studies. We considered these interpretations in our analysis of the proposed proprietary name.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, February 7, 2013 e-mail, the Division of Psychiatry Products (DPP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Vraylar. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Vraylar, identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified in the (b) (4) external name study, not identified by DMEPA, which require further evaluation.

Table 1: Collective List of Potentially Similar Names from DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study if applicable

Look Similar (n=27)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Verelan	EPD Panel	Zemplar	EPD Panel	(b) (4) ***	EPD Panel
Uroplus	EPD Panel	Uvadex	EPD Panel	Viadur	EPD Panel
Viactiv	EPD Panel	Vayarol	EPD Panel	Naftin	EPD Panel
Urealac	EPD Panel	Virazole	EPD Panel	(b) (4)	EPD Panel
Nicolar	EPD Panel	Unasyn	EPD Panel	Uroxatrol	(b) (4)
Uracid	EPD Panel	Reglan	(b) (4)	Valtrex	(b) (4)
Viagra	EPD Panel (b) (4)	Valcyte	(b) (4)	Vyvanse	(b) (4)
Valium	(b) (4)	Varenicline	(b) (4)	Orazinc	Primary Safety Evaluator
Zymar	(b) (4)	Raybar	Primary Safety Evaluator	(b) (4) ***	Primary Safety Evaluator
Sound Similar (n=5)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Cefaclor	(b) (4)	Sular	(b) (4)	Fanapt	Primary Safety Evaluator
Verapamil	(b) (4)	Valacyclovir	(b) (4)		

Look and Sound Similar (n=4)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Vrailar	EPD Panel	Viibryd	(b) (4)		
(b) (4) ***	EPD Panel	Vytorin	EPD Panel (b) (4)		

Our analysis of the 36 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 36 names will not pose a risk for confusion as described in Appendices D through E.

2.2.8 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Psychiatry Products via e-mail on March 20, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Psychiatry Products on March 26, 2013, they stated no additional concerns with the proposed proprietary name, Vraylar.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Sandra Rimmel, OSE Project Manager, at 301-796-445.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Vraylar, and have concluded that this name is acceptable. The proposed proprietary name will be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change. If any of the proposed product characteristics as stated in your January 17, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

1. ***Micromedex Integrated Index (http://csi.micromedex.com)***

   Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)***

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

   DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

   This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. ***Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)***

   Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. ***U.S. Patent and Trademark Office (http://www.uspto.gov)***

   USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)***

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. ***Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)***

   The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

10. ***Natural Medicines Comprehensive Databases (www.naturaldatabase.com)***

    Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

11. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

13. ***Red Book (www.thomsonhc.com/home/dispatch)***

    Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

14. ***Lexi-Comp (www.lexi.com)***

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

15. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

16. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

18. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. ***Dogpile (www.dogpile.com)***

    Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

20. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). 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. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

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

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. 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.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[3] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

[3] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

Moreover, DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Vraylar	Scripted May Appear as	Spoken May Be Interpreted as
V, v	b, C, J, L, M, r, U, X, Y, y	B, F, Ph, R
r	s, n, e, v	
a	el, ci, cl, d, o, u	e, i
y	f, g, j, p, u, v, x, Z	a, i, m
l	b,e, s, P, i	
a	el, ci, cl, d, o, u	e, o
r	s, n, e, v	
Letter strings		
Vray	Rhay, Vry, Viay, Vrai, Vhay	Bray, Brey, Brai, Brei, Fra, Fre, Fram, Ray, Vey, Vra, Vre, Vue, Vrei, Vyra
lar		lahr, lehr

Appendix C: Prescription Simulation Samples and Results

Figure 1. Vraylar Study (Conducted on February 8, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Inpatient Medication Order: Vraylar (b) (4) po qday	Vraylar 4.5 mg 1 capsule daily Disp. #30
Outpatient Prescription: Vraylar 4.5mg 1 cap daily #30	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

				192 People Received Study 93 People Responded
Study Name: Vraylar				
Total	**31**	**28**	**34**	
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
FRALAR	0	1	0	1
FRAMAR	0	1	0	1
FRAMLAR	0	1	0	1
FRAMOR	0	1	0	1
FRAYLAR	0	4	0	4
FRELAR	0	1	0	1
RAYLAR	0	2	0	2
RELAR	0	1	0	1
RHAYLAR	0	0	1	1
V RAYLAR	0	0	1	1
VHAYLAR	0	0	2	2
VIAYLAR	1	0	0	1
VRAILAR	0	1	0	1
VRALAR	0	5	0	5
VRALOR	0	1	0	1
VRAYLAR	29	7	30	66
VRYLAR	1	0	0	1
VUELAR	0	1	0	1
VYRALAR	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Drug Name	Active Ingredient	Similarity to Vraylar	Failure preventions
1.	Vytorin	Ezetimibe and Simvastatin	Look	The pair have sufficient orthographic differences.
2.	Naftin	Naftifine Hydrochloride	Look	The pair have sufficient orthographic differences.
3.	Unasyn	Ampicillin and Sulbactam	Look	The pair have sufficient orthographic differences.
4.	Uroxatrol	Alfuzosin Hydrochloride	Look	The pair have sufficient orthographic differences.
5.	Valcyte	Valganciclovir	Look	The pair have sufficient orthographic differences.
6.	Valium	Diazepam	Look	The pair have sufficient orthographic differences.
7.	Valtrex	Valacyclovir Hydrochloride	Look	The pair have sufficient orthographic differences.
8.	Varenicline	Varenicline Tartrate	Look	The pair have sufficient orthographic differences.
9.	Vyvanse	Lisdexamphetamine Dimesylate	Look	The pair have sufficient orthographic differences.
10.	Zymar	Gatifloxacin	Look	The pair have sufficient orthographic differences.
11.	Viactiv	Family Tradename: Viactiv Calcium Plus D Viactiv Multi-Vitamin	Look	The pair have sufficient orthographic and/or phonetic differences.
12.	Valacyclovir	Valacyclovir Hydrochloride	Sound	The pair have sufficient phonetic differences.
13.	Cefaclor	Cefaclor	Sound	The pair have sufficient orthographic differences.
14.	Sular	Nisoldipine	Sound	The pair have sufficient phonetic differences.
15.	Verapamil	Verapamil Hydrochloride	Sound	The pair have sufficient phonetic differences.
16.	Fanapt	Iloperidone	Sound	The pair have sufficient phonetic differences.
17.	Viibryd	Vilazodone Hydrochloride	Look and Sound	The pair have sufficient orthographic and/or phonetic differences.

18.	Uracid	Racemethionine	Look	Full product characteristic information not available in our usual drug information databases.
19.	Viadur	Leuprolide Acetate	Look	This product has been discontinued. There are no generics available.
20.	Uradan	Unknown	Look	This name was identified in USPTO. The name was owned by Medimetriks Pharmaceuticals. According to USPTO the name has been abandoned and is now "dead". This name was not identified in our other drug information databases and has not been submitted to the Agency for review.
21.	(b) (4)	Tipranavir	Look	(b) (4) *** was a proposed name for Tipranavir. The NDA was approved under the name Aptivus.
22.		Doxycycline	Look	This proposed name was withdrawn by the Applicant. The ANDA was approved without a proprietary name.
23.	Raybar	Barium Sulfate	Sound	This name was identified in Micromedex. Full product characteristic information could not be found in Micromedex or any of our usual drug information databases.
24.	Vrailar	None	Look and Sound	The name was identified in USPTO. It is owned by Forest Laboratories who is the Applicant for Vraylar, the name that is the subject of this review. The name Vrailar was not identified in our usual drug information databases and does not appear to be a name that is currently marketed. Additionally, Vrailar is currently not a proposed alternate name.
25.	(b) (4) ***	Aclidinium Bromide	Look and Sound	(b) (4) *** was an alternate proposed name for Aclidinium Bromide. The NDA was approved under the name Tudorza Pressair.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/or use in clinical practice for the reasons described.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
26.	Zemplar (Paricalcitol) Capsules Injection Strengths: *Capsules:* 1 mcg, 2 mcg, and 4 mcg *Injection:* 2 mcg/mL (1 mL vial) 5 mcg/mL (1 mL and 2 mL vials) Dosage: *Oral:* 1 mcg or 2 mcg orally once daily; 2 mcg or 4 mcg orally three times per week *Injection:* Initial dosage: 0.04 to 0.1 mcg/kg (2.8 to 7 mcg) intravenous bolus dose no more frequently than every other day at any time during dialysis; Dose titration: If a satisfactory response is not observed, the dose may be increased by 2 to 4 mcg at 2 to 4-week intervals	Orthographic: The beginning letters "V" and "Z" look similar when written. Both names contain a downstroke letter in the fourth position ("y" vs. "p") followed by the identical suffix "lar". Dose: Zemplar injection is given by weight based dosing; therefore, the potential exists for numerical overlap in dose (e.g., 3 mcg vs. 3 mg) between intravenous Zemplar and Vraylar. Frequency and Route of Administration: Both products can be administered orally once daily	Orthographic: The infixes "ra" vs. "em" look different.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
27.	Reglan (Metoclopramide) Tablets Injection (discontinued, generics available) Strengths: *Tablets:* 5 mg and 10 mg *Oral Solution:* (discontinued, generics available): 1 mg/mL *Injection:* 5 mg/mL Dosage: *Oral:* 10 mg to 15 mg orally up to four times per day; 20 mg orally prior to the provoking gastrointestinal situation *Intravenous or Intramuscular:* Post-operative nausea and vomiting: 10 mg to 20 mg intramuscularly Chemotherapy induced nausea and vomiting: 1 mg/kg to 2 mg/kg as in intravenous infusion over 30 minutes before chemotherapy, repeat every 2 hours for two times, then every 3 hours for three times	Orthographic: The beginning letters "V" vs. "R" look similar when written in lower case. The suffixes "ylar" vs. "glan" look similar when written. Dose: There is potential for numerical similarity between doses of the products (i.e. 1.5 mg vs. 15 mg).	Orthographic: Although the beginning letters "v" and "r" may look similar, the infixes "ra" vs. "e" look different when written.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
28.	Verelan (Verapamil HCl) Extended-release capsules Strengths: 120 mg, 180 mg, 240 mg, and 360 mg Dosage: 120 mg to 480 mg orally once daily	Orthographic: Both names begin with the letter "V". The suffixes "lar" and "lan" look similar. (b) (4) Route of administration and frequency of administration: Both products are administered orally once daily.	Orthographic: The infixes "ere" and "ray" look different when scripted. Vraylar contains the downstroke letter "y" whereas Verelan does not contain any downstroke letters.
29.	Urealac (Urea) Lotion, Nailstick Topical Solution, Cream Nail, Gel, Ointment, Suspension Lotion 35% The strength of all other dosage forms is 50% Dosage: Dosage information specific to these products could not be found; however, similar products are typically applied topically in a sufficient amount to the affected area(s) twice daily.	Orthographic: Both names contain seven letters. The beginning letter strings "Vr" and "Ur" and the suffixes "lar" and "lac" look similar when written.	Orthographic: Vraylar contains a downstroke "y" whereas Urealac does not contain any downstroke letters. Dosage form: Capsules vs. Lotion, Nailstick Topical Solution, Cream Nail, Gel, Ointment, Suspension The dosage form would have to be specified on a Urealac prescription because it is available in multiple dosage forms. Vraylar and Urealac do not have overlapping dosage forms.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
30.	Nicolar (Niacin) Tablets Strength: 500 mg Dosage: 500 mg to 2 g orally twice daily or three times per day	Orthographic: The beginning letters "V" vs. "N" look similar when written. Both names contain the suffix "lar". Dosage form and route of administration: Both products are solid oral dosage forms administered orally.	Orthographic: The infixes "ico" vs. "ray" look different when written. Strength: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) (multiple strengths) vs. 500 mg (single strength) Vraylar is available in multiple strengths so the strength would have to be written on a prescription for it whereas Nicolar is available in a single strength so a prescription for it does not have to have a strength specified. Additionally, the products do not have overlapping strengths.
31.	Vayarol (Phytosterol Esters, Docosahexaenoic Acid, and Eicosapentaenoic Acid) Capsules Strength: 630 mg/232.5 mg/ 92.5 mg per capsule Dosage: 2 capsules per day	Orthographic: Both names begin with the letter "V" and contain the infix letters "ay" in the beginning portion of the name. Dosage form, route of administration, and frequency: Both products are capsules that can be administered orally once per day	Orthographic: The suffixes "lar" vs. "arol" look different when written. Strength: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) (multiple strengths) vs. 630 mg/232.5 mg/ 92.5 mg (single strength) Vraylar is available in multiple strengths so the strength would have to be written on a prescription for it whereas Vayarol is available in a single strength so a prescription for it does not have to have a strength specified. Additionally, the products do not have overlapping strengths.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
32.	Uradex (Methoxsalen) Injection Strength: 20 mcg/mL (20 mL vial) Dosage: 200 mcg extracorporeally on two consecutive days every 4 weeks; or on two consecutive days every 2 weeks	Orthographic: The prefixes "Vra" vs. "Uva" look similar when written	Orthographic: The suffixes "ylar" vs. "dex" look different when written. Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) vs. 200 mcg The products do not overlap in dose.
33.	Virazole (Ribavirin) for Inhalation Solution Strength: 6 gm per vial Dosage: 20 mg/mL solution (after reconstitution) via continuous aerosol administration for 12 to 18 hours per day	Orthographic: Both names begin with the letter "V" and contain the letter "a" followed by a downstroke letter "y" vs. "z". Both names contain an upstroke letter "l" in the suffix of the name. Strength: There is numerical overlap between product strengths (6 mg vs. 6 g)	Orthographic: The suffixes "lar" vs. "ole" look different when written. Frequency of administration: Once daily vs. continuous aerosol for 12 to 18 hours per day.
34.	Orazinc (Zinc Sulfate) Tablets Strengths: 110 mg and 220 mg Dosage: 110 mg or 220 mg orally once daily	Orthographic: The prefixes "Vray" vs. "Oraz" look similar when written. Dosage form, route of administration, and frequency of administration: Both products are solid oral dosage forms administered orally once daily.	Orthographic: The suffixes "lar" vs. "inc" look different when scripted. Strength: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) vs. 110 mg and 220 mg The products do not have overlapping strengths.

	Proposed name: Vraylar (Cariprazine) Capsules	**Strengths: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4)**	**Usual Dose: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) orally once daily**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
35.	Uroplus SS Uroplus DS (Sulfamethoxazole and Trimethoprim) Tablets Strength: SS: 400 mg/80 mg DS: 800 mg/160 mg Dosage: *SS:* 2 to 4 tablets orally once daily, twice daily or four times per day, depending on the indication *DS:* 1 to 2 tablets orally once daily, twice daily or four times per day, depending on the indication	Orthographic: The letters in Vraylar look similar to the letters in the root name Uroplus in all of the individual letter positions because both names contain upstroke and downstroke letters in the same positions. Additionally, the letters "r" and "l" are in the same positions in both names. Dosage form, route of administration, and frequency of administration: Both products are solid oral dosage forms administered orally that can also be administered once daily.	Orthographic: The modifiers "SS" and "DS" help to differentiate the names. Strength: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) (multiple strengths) vs. 400 mg/80 mg (SS) or 800 mg/160 mg (DS) There are no overlapping strengths between these products.
36.	Viagra (Sildenafil Citrate) Tablets Strengths: 25 mg, 50 mg, and 100 mg Dosage: 25 mg to 100 mg orally once daily 4 hours to ½ hour prior to sexual activity	Orthographic: Both names begin with the letter "V". Both names contain the letter "a" in the third position, and a downstroke letter ("y" vs. "g") in the fourth position Dosage form and route of administration: Both products are solid oral dosage forms administered orally.	Orthographic: Vraylar contains an upstroke letter 'l' whereas Viagra does not contain any upstroke letters. Strength: 1.5 mg, 3 mg, 4.5 mg, 6 mg, (b) (4) vs. 25 mg, 50 mg, and 100 mg The products do not have overlapping strengths.

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