CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219016Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	February 5, 2024
Application Type and Number:	NDA 219016
Product Name and Strength:	Edurant PED (rilpivirine) tablets for oral suspension, 2.5 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Janssen Research and Development, LLC (Janssen)
PNR ID #:	2023-1044725456
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Acting Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Edurant PED, 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. Janssen did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Edurant (rilpivirine) was approved on May 20, 2011 and is currently marketed as 25 mg tablets under NDA 202022.

Under NDA 219016, Janssen proposes a new 2.5 mg tablet for oral suspension formulation of rilpivirine and requested review of the proposed proprietary name, Edurant PED, for the new formulation.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 7, 2023.

Table 1. Relevant Product Information for Edurant PED and Edurant

	Edurant PED (proposed product)	**Edurant** [a]
Initial Approval Date	N/A	May 20, 2011
Intended Pronunciation	ee' dur and ped	ee' dur and
Active Ingredient	rilpivirine	
Indication of Use	In combination with other antiretroviral agents, for the treatment of HIV-1 infection in treatment-naïve patients 2 years of age and older and weighing at least 10 kg with HIV-1 RNA less than or equal to 100,000 copies/mL	
Route of Administration	Oral	
Dosage Form	tablets for oral suspension	tablet
Strength	2.5 mg	25 mg
Dose and Frequency	Weight-based dosing administered by mouth once daily 10 kg to less than 20 kg- 12.5 mg (5 x 2.5 mg tablets for oral suspension	Treatment Naive Patients-One 25 mg tablet once daily Treatment in Combination with Cabotegravir- One 25 mg tablet in

[a] Product information obtained at: DailyMed - EDURANT- rilpivirine tablet, film coated (nih.gov)Accessed December 1, 2023.

	20 kg to less than 25 kg-15 mg (6 x 2.5 mg tablets for oral suspension	combination with 30 mg tablet of Vocabria Dosage with Rifabutin- 50 mg (2x 25 mg tablets) once daily
How Supplied	Blister cards of 10 tablets with 9 blisters per carton	Bottles of 30 tablets
Storage	Store at 20-25°C (68-77°F); with excursions permitted to 15°-30°C (59°-86°F) [see USP controlled room temperature].	Store at 25°C (77°F); excursions permitted 15° to 30°C (59° to 86°F). [See USP Controlled Room Temperature].

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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

The proposed proprietary name, Edurant PED, is comprised of the root name, Edurant, and the modifier, "PED." The root name, Edurant, is currently marketed. Janssen indicates that the modifier, "PED," is intended to denote "the specific pediatric formulation of 2.5 mg tablets," as a differentiator for prescribers.

2.2.3 Comments from Other Review Disciplines at Initial Review

The Division of Antivirals (DAV) did not forward any comments or concerns relating to Edurant PED at the initial phase of the review.

[b] USAN stem search conducted on November 29, 2023.

2.2.4 FDA Name Simulation Studies

Seventy-six (n=76) practitioners participated in DMEPA's prescription studies for Edurant PED. One participant identified Enduron in the CPOE study. However, it appears that this participant entered an incorrect sequence of letters, 'End' instead of 'Edu,' when searching for the study name. As a result, the CPOE generated a pick list that did not contain Edurant PED as a choice. The participant proceeded to incorrectly select Enduron as their response. Thus, in this case, it appears the participant attempted to select an answer that was closest to the response needed given the goal of the simulated study. This name pair has sufficient phonetic and orthographic differences, with a combined POCA score of 50%, suggesting low similarity between Edurant PED and Enduron. Furthermore, we note that Enduron (NDA 012524) is discontinued with no generic equivalents available (FR withdrawn 4/18/2012). Based on these factors, we determined the risk for a medication error between this name pair is adequately minimized.

Appendix B contains the results from the prescription simulation studies.

2.2.5 Safety Assessment of the Proposed Name Edurant PED

In this section, we provide a safety analysis of the proposed proprietary name Edurant PED. Janssen currently markets Edurant (rilpivirine), approved on May 20, 2011 as 25 mg tablets, for patients 12 years of age and older and weighing at least 35 kg. Under NDA 219016, Janssen proposes a new 2.5 mg tablet for oral suspension formulation of rilpivirine, revising the indication to patients 2 years of age and older and weighing at least 10 kg. Janssen proposes to differentiate the proposed 2.5 mg rilpivirine tablet for oral suspension formulation from the currently marketed tablet formulation using the modifier "PED." As such, we evaluated the following: (1) use of the same root name, (2) use of a modifier to distinguish the products, and (3) the proposed modifier "PED".

1. Evaluation of the use of the same root name, "Edurant"

We note that Edurant and Edurant PED have the same active ingredient, indication (treatment of HIV-1), and route of administration (oral). Our postmarket surveillance has not identified any medication errors attributed to name confusion involving Edurant. Therefore, we do not object to the use of the same root name, Edurant, for this proposed product.

2. Evaluation of the use of a modifier to differentiate the products

Janssen proposes to differentiate the proposed product, Edurant PED, from the currently marketed Edurant, by using a modifier in the proposed proprietary name nomenclature. It is not uncommon to use modifiers to denote a specific product formulation as part of a product line extension. However, we note that both Edurant and Edurant PED would be supplied in a single strength (25 mg *versus* 2.5 mg) which differs by 10-fold. Both products are administered by a single, oral route of administration and are available in a single dosage form (tablets for oral suspension *versus* tablets). Thus, we note that a prescription could be written without the strength, route of administration, or dosage form included; for example, "Edurant PED 5 tablets once daily." If this occurs, a prescription intended for Edurant PED, could be misinterpreted as "Edurant 5 tablets once daily" where Edurant tablets are dispensed or administered in place of Edurant PED tablets for oral suspension, resulting in an overdose. We also note that due to the 10-fold difference in strength between Edurant and Edurant PED (25 mg *versus* 2.5 mg), there is a risk that the strength is misinterpreted on a prescription/medication order. For example, a

prescription for “Edurant 25 mg once daily” may be misinterpreted as “Edurant 2.5 mg once daily” where Edurant PED is dispensed, resulting in an underdose.

We note that such errors could occur if the modifier were omitted or overlooked as the omission and oversight of a modifier is cited in literature as a common cause of medication errors.[c] Postmarketing experience shows that the introduction of product line extensions may result in medication errors if the modifier is omitted, and the product characteristics are similar or overlap.

To better understand the clinical consequences to such error and to further assist us in our evaluation of the proposed name, we note the following information included in NDA submission:

- Edurant and Edurant PED would not be substitutable on a mg-per-mg basis.
- The proposed dosing for Edurant PED Tablets for Oral Suspension is weight-based administered once daily as follows:
    - 10 kg to less than 20 kg: 12.5 mg (5 x 2.5 mg tablets for oral suspension)
    - 20 kg to less than 25 kg: 15 mg (6 x 2.5 mg tablets for oral suspension)

Janssen indicates that the modifier, “PED,” is intended to denote “the specific pediatric formulation of 2.5 mg tablets,” as a differentiator for prescribers. However, the use of the wrong formulation could lead to overdose (i.e., if Edurant tablets are inadvertently administered in place of Edurant PED tablets for oral suspension) or underdose errors (i.e., if Edurant PED tablets for oral suspension are inadvertently administered in place of Edurant tablets). We note that the difference in dosing between the products (e.g., Edurant 1 or 2 tablets once daily *versus* Edurant PED 5 or 6 tablets once daily), tablet and packaging appearance, use of electronic prescribing practices and labeling strategies (i.e., differentiation in the US Prescribing Information, container label, and carton labeling) could help to minimize name confusion between the two products. Labeling considerations for this product will be addressed under separate cover.

Although we acknowledge that modifiers may be omitted or overlooked; when used, they can assist in differentiating products and may help to prevent potential product selection errors. Furthermore, the difference in dosing between the products Edurant and Edurant PED provides an added measure of safety. We considered multiple failures would need to occur simultaneously in order for Edurant tablets to be administered in place of Edurant PED tablets for oral suspension or vice versa (e.g., omission or overlooking the modifier AND failure to recognize the difference in dosing between Edurant and Edurant PED).

We note that Triumeq PD and Tivicay PD have similar naming conventions and therefore, we conducted a FAERS search of the name pairs, Triumeq/Triumeq PD and Tivicay/Tivicay PD, on December 13, 2023 to determine whether the naming strategy resulted in any medication errors involving the wrong product dispensed (between Triumeq/Triumeq PD and Tivicay/Tivicay PD), or reports of modifier confusion or misinterpretation. Our search did not identify reports of medication errors as described.

An alternative to using a modifier to distinguish this proposed product from the currently marketed product is to use a different proprietary name (i.e., one that does not use the root name Edurant). However, marketing the new product under a unique proprietary name still carries the

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

risk of medication errors, specifically, those associated with therapeutic duplication and subsequent overdoses, if the proprietary names are not recognized as having the same active ingredient. These errors may have greater associated safety risks than the omission or oversight of the modifier as discussed above.

Thus, based on the totality of this information, we do not object to the use of a modifier for this product as a naming strategy to differentiate the products.

3. Evaluation of the proposed modifier "PED"

According to Janssen, the modifier "PED" is intended to denote "the specific pediatric formulation of 2.5 mg tablets" for Edurant PED. We note that the modifier 'PED' is not on the Institute of Safe Medication Practices' (ISMP) List of Products with Drug Name Suffixes[d]. However, the modifier "PED" has been incorporated in other marketed products, including Lupron Depot-PED (NDA 020263), Ery-PED (NDA 050297) and several OTC liquid formulations (G-Tron PED, G-Tuss-NL PED and Biocotron- PED) to signify pediatric formulations.

We also note that Edurant PED will be supplied as a tablet for oral suspension, which is intended to achieve dosing in the pediatric population, and thus is not misleading. Therefore, we do not object to the use of the modifier "PED" for this product.

In summary, given the totality of the factors considered above, we conclude that the use of the root name Edurant and the proposed modifier, "PED," though still vulnerable to some risk of medication error, offers an acceptable approach in naming this particular product.

2.2.6 Communication of DMEPA's Determination

On February 5, 2024, DMEPA 1 communicated our determination to the Division of Antivirals (DAV).

3 CONCLUSION

The proposed proprietary name, Edurant PED, is conditionally acceptable.

If you have any questions or need clarifications, please contact Danyal Chaudhry, OSE project manager, at 301-796-3813.

3.1 COMMENTS TO JANSSEN RESEARCH AND DEVELOPMENT, LLC

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

If any of the proposed product characteristics as stated in your submission, received on November 7, 2023.

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

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. [e]

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

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

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

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

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

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

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

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

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

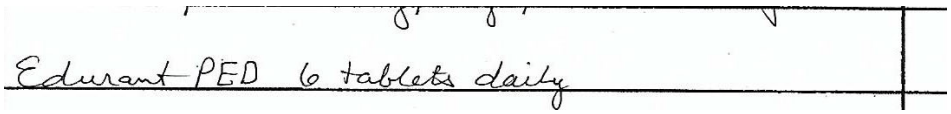
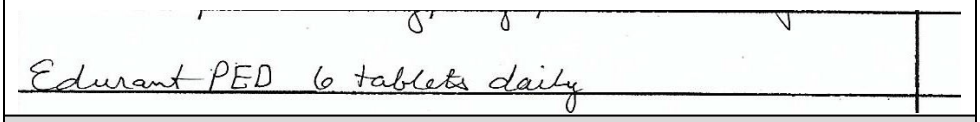
The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Edurant PED Study (Conducted on December 8, 2023)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Edurant PED 2.5 mg Disperse 5 tablets in water and administer once daily
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Edurant PED	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Edurant PED - 2023-12-08

People Received Study: 167

People Responded: 76

Total	18	20	14	24	76
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
EDERANTHEAD	0	0	1	0	1
EDERONT PED	0	0	1	0	1
EDERRONT PEG	0	0	1	0	1
EDIMONT PED	0	1	0	0	1
EDORANT PAD	0	0	1	0	1
EDORANT-PED	0	0	1	0	1
EDORONT PAD	0	0	1	0	1
EDURANT FED	0	1	0	0	1
EDURANT PED	16	15	4	23	58
EDURANT PED 2.5 MG TABLETS FOR ORAL SUSPENSION	0	1	0	0	1

EDURANT PED 2.5MG FOR ORAL SUSPENSION	0	1	0	0	1
EDURANT PED FOR ORAL SUSPENSION	0	1	0	0	1
EDURNAT PED	1	0	0	0	1
EEDERONT TED	0	0	1	0	1
EEDURANT PED	0	0	1	0	1
ENDURANT PED	1	0	0	0	1
ENDURON	0	0	0	1	1
ETHERUNT PED 2.5 MG TABLET FOR ORAL SUSPENSION.	0	0	1	0	1
IDERANT PEG	0	0	1	0	1

APPEARS THIS WAY ON ORIGINAL

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/

MADHURI R PATEL on behalf of MELINA N FANARI
02/05/2024 12:38:35 PM

MADHURI R PATEL
02/05/2024 12:43:52 PM

MISHALE P MISTRY
02/05/2024 01:52:13 PM