CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214275Orig1s000

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:	February 16, 2021
Application Type and Number:	NDA 214275
Product Name and Strength:	Uptravi (selexipag) for injection, 1,800 mcg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Actelion Pharmaceuticals Us Inc (Actelion)
Panorama #:	2020-44039668
DMEPA Safety Evaluator:	Mariette Aidoo, PharmD, MPH
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director of Nomenclature and Labeling:	Chi-Ming (Alice) Tu

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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Uptravi (selexipag) tablets were approved on December 21, 2015, under NDA 207947. Uptravi tablets are a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Actelion submitted the name, Uptravi, for the newly proposed dosage formulation (i.e., for injection) for review of NDA 214275 on November 23, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the November 23, 2020 proprietary name submission, the proposed Prescribing Information for Uptravi injection submitted on September 9, 2020, and the Prescribing Information for Uptravi (selexipag) tablets.

Table 1. Relevant Product Information for Selexipag		
Product	**Uptravi (NDA 214275)**	**Uptravi [a] (NDA 207947)**
Initial Approval Date	Under review	December 21, 2015
Intended Pronunciation	up-TRA-vee	
Active Ingredient	selexipag	
Indication	Treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.	
Route of Administration	Intravenous infusion	Oral
Dosage Form	For Injection	Tablets
Strength	1,800 mcg/vial	200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,000 mcg, 1,200 mcg, 1,400 mcg and 1,600 mcg
Dose and Frequency§	• UPTRAVI for injection dose is determined by the patient's current	• Initial dose: 200 mcg twice daily.

[a] Uptravi (selexipag) [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2021 JAN 12. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/2015/207947s000lbl.pdf

	dose of UPTRAVI tablets when patients are temporarily unable to take oral therapy. • UPTRAVI® for injection must be administered by intravenous infusion, twice daily. • (b) (4) .	• Increase the dose by 200 mcg twice daily at weekly intervals to the highest tolerated dose up to 1600 mcg twice daily. • Maintenance dose is determined by tolerability. • Moderate hepatic impairment: Starting dose 200 mcg once daily, increase the dose by 200 mcg once daily at weekly intervals to the highest tolerated dose up to 1600 mcg.
Preparation and Administration	• UPTRAVI® for injection must be reconstituted and then further diluted prior to administration by intravenous infusion, at the appropriate infusion rate, using only 0.9% sodium chloride for injection. • (b) (4)	Do not split, crush, or chew tablets.
How Supplied	• UPTRAVI® for Injection: 1,800 mcg as a lyophilized powder [white to almost white broken cake or powdered material] in a single-dose 10 mL Type I glass vial closed by a stopper and sealed with an aluminum flip-off button for reconstitution and dilution.	• UPTRAVI® Film-Coated Tablets [200 mcg, 400 mcg, 600 mcg, 800 mcg, 1000 mcg, 1200 mcg, 1400 mcg and 1600 mcg]. • UPTRAVI® Titration Pack: includes a 140 count bottle of 200 mcg tablets and a 60 count bottle of 800 mcg tablets.
Storage	Before reconstitution: refrigerate the glass vial package before use from 2°C to 8°C (36ºF to 46ºF) in the original package in order to protect from light. After reconstitution: Maximal holding time at room temperature after first puncturing of the stopper of the vial is 4 hours including the time required for administration	Store at 20ºC to 25ºC (68ºF to 77ºF). Excursions are permitted between 15°C and 30°C (59°F and 86°F) [*see USP Controlled Room Temperature*].
Care Environment for Dispensing and Use	(b) (4)	(b) (4)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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

Actelion did not provide a derivation or intended meaning for the proposed proprietary name, Uptravi, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, December 16, 2020 e-mail, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Uptravi at the initial phase of the review.

2.2.4 Multiple Dosage Forms Under a Single Proprietary Name

Under NDA 214275, the Applicant proposes selexipag for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. The Applicant proposes the use of Uptravi for injection in patients who are currently treated with Uptravi tablets but are temporarily unable to take oral therapy. With this NDA, the Applicant proposes a new "for injection" dosage form of selexipag in a 1,800 mcg/vial dosage strength, to be marketed under the same name as the currently approved product, Uptravi.

We note that the newly proposed dosage form shares the same active ingredient, indication, and frequency as the currently approved Uptravi tablets. We also note that the recommended dose of

[b] USAN stem search conducted on December 28, 2020.

Uptravi for injection is 12.5% higher than the patient's current oral dose of Uptravi tablets (*see Appendix B*). In addition, the Applicant proposes to market both the currently approved Uptravi tablets and the newly proposed Uptravi for injection under the same Prescribing Information.

It is a common and accepted practice to have multiple dosage forms of an active ingredient managed under one proprietary name. In the case of Uptravi, the residual risk of confusion between the 2 dosage formulations of the product may be mitigated through labels and labeling intervention.

Furthermore, we note that through our routine monitoring we have not identified any medication errors involving name confusion with the proprietary name Uptravi. Therefore, given the precedence for using this naming convention, and the absence of any medication errors involving the proprietary name, we find the Sponsor's proposal to market the proposed product with the proprietary name Uptravi acceptable.

2.2.5 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiology and Nephrology (DCN) via e-mail on February 9, 2021. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Cardiology and Nephrology (DCN) on February 11, 2021, they stated no additional concerns with the proposed proprietary name, Uptravi.

3 CONCLUSION

The proposed proprietary name, Uptravi, is acceptable.

If you have any questions or need clarifications, please contact Wana Manitpisitkul, OSE project manager, at (240) 402-4156.

3.1 COMMENTS TO ACTELION PHARMACEUTICALS US INC

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

A request for proprietary name review for Uptravi should be submitted once your marketing application is submitted.

If any of the proposed product characteristics as stated in your submission, received on November 23, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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 DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [c]

[c] National Coordinating Council for Medication Error Reporting and Prevention. 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.

Appendix B: Dosage and Administration Information for Uptravi (selexipag) Infusion submitted 09/29/2020[d]

Table 2: Dosing Table for UPTRAVI intravenous based on current UPTRAVI tablets dose

UPTRAVI tablets dose (mcg) for twice daily dosing	Corresponding IV UPTRAVI Dose (mcg) for twice daily dosing	Reconstituted transfer volume (mL) for dilution	0.9% sodium chloride solution, volume (mL) for dilution in a glass container	Total volume available for infusion (mL)	Infusion Rate mL per hour[a]
200	**225**	**1.0**	**100**	**101**	**75.8**
400	**450**	**2.0**	**100**	**102**	**76.5**
600	**675**	**3.0**	**100**	**103**	**77.3**
800	**900**	**4.0**	**100**	**104**	**78.0**
1000	**1125**	**5.0**	**100**	**105**	**78.8**
1200	**1350**	**6.0**	**100**	**106**	**79.5**
1400	**1575**	**7.0**	**100**	**107**	**80.3**
1600	**1800**	**8.0**	**100**	**108**	**81.0**

[a] Ensure entire contents from the glass container and IV tubing are infused at the indicated rate

[d] Uptravi (selexipag) [Prescribing Information]. 2020 SEP 29. Available from: \\CDSESUB1\evsprod\nda214275\0001\m1\us\selexipag-draft-labeling-text-clean.pdf

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