CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209279Orig1s000

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:	August 16, 2017
Application Type and Number:	NDA 209279
Product Name and Strength:	Tracleer (Bosentan) tablets for oral suspension, 32 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Actelion Pharmaceuticals LTD
Panorama #:	2017- 16384993
DMEPA Primary Reviewer:	Sarah Thomas, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Tracleer 62.5 mg and 125 mg tablets were approved on November 20, 2001 under the proprietary name, Tracleer (NDA 021290). The Applicant now seeks the new dosage formulation 32 mg tablet for oral suspension under NDA 209279 for pediatric use. The Applicant submitted the proposed proprietary name, Tracleer, for review for NDA 209279 on July 14, 2017.

1.2 PRODUCT INFORMATION

The following product information is provided in the July 14, 2017 proprietary name submission.

- Intended Pronunciation: tra-KLEER
- Active Ingredient: Bosentan
- Indication of Use: Tracleer® is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):
    - in pediatric patients aged 3 years and older with idiopathic or congenital pulmonary arterial hypertension (PAH) to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.
- Route of Administration: Oral
- Dosage Form: Tablets for oral suspension (scored)
- Strength: 32 mg
- Dose and Frequency:

	Initial 4 weeks	Maintenance (after 4 weeks)
Patients > 12 years of age and >40 kg	62.5 mg twice daily	125 mg twice daily
Patients > 12 years of age and <40 kg	62.5 mg twice daily	62.5 mg twice daily
Patients ≤12 years of age		
≥4-8 kg	16 mg twice daily	16 mg twice daily
>8-16 kg	32 mg twice daily	32 mg twice daily
>16-24 kg	48 mg twice daily	48 mg twice daily
>24-40 kg	64 mg twice daily	64 mg twice daily

- How Supplied: Carton of 56 tablets for oral suspension in 4 blister-strips of 14 tablets
- Storage: Store at 20ºC – 25ºC (68ºF – 77ºF). Excursions are permitted between 15°C and 30°C (59°F and 86°F). [See USP Controlled Room Temperature]. These storage temperatures apply to both film-coated and dispersible tablets. Divided dispersible tablets should be stored under the same conditions and used within 7 days. Tablet pieces may be returned to the opened blister and stored there out of reach of children for up to 7 days.
- Container and Closure Systems: Packaged in child resistant Aluminum/Aluminum peel-push blisters

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 Cardiovascular and Renal Products (DCRP) 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[a].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Tracleer 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, July 26, 2017 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.1 Names with Strength Overlap and Potential Orthographic, Spelling, and Phonetic Similarities

The proposed product, Tracleer will be available in a 32 mg strength, in addition to the already marketed 62.5 mg and 125 mg strengths. Since the 32 mg is not a typical strength that is commonly marketed, we searched the Electronic Drug Registration and Listing System (eDRLS) database to identify names with strength overlap. There were no names of concern with strength

[a] USAN stem search conducted on July 14, 2017.

overlap and potential orthographic, spelling, and phonetic similarities with Tracleer. Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences are listed in Appendix I.

2.2.2 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Tracleer*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	July 13, 2017
Drug Name	Tracleer [product name] All "Tracleer" verbatim names under Product Verbatim field
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Event PT	Medication Error
Date Limits	N/A

Our FAERS search retrieved 43 cases. Each case report was reviewed for relevancy to this proprietary name review. After individual review, we did not identify any medication errors associated with Tracleer name confusion.

2.2.3 Multiple Dosage Forms under a Single Proprietary Name

Tracleer is currently marketed under NDA 021290 as tablets in strengths of 62.5 mg and 125 mg. We considered the appropriateness of using the proprietary name, Tracleer, for the new 32 mg tablets for oral suspension under NDA 209279. We note that the Tracleer tablets and the proposed tablets for oral suspension share the same active ingredient (Bosentan) and PAH indication.

Per Actelion's July 14, 2017 proprietary name submission, the 32 mg tablet for oral suspension is intended to be utilized in the pediatric PAH population. While we recognize that the proposed dosing and dosage form choice is by patients' age (patients less than 12 years old use the proposed tablet for oral suspension), if marketed under the same proprietary name, then we anticipate prescribers may prescribe the proposed tablet for oral suspension for adult patients who have been on Tracleer tablets but have difficulty swallowing. For example, prescribers may prescribe two or four 32 mg tablets for oral suspension (64 mg and 128 mg) to mimic the 62.5 mg and 125 mg tablets adult dosing. Given this concern, we discussed the potential clinical/therapeutic effects with the Review Team. Per email communication on July 25, 2017, the Review Team confirmed the systemic exposure following the administration of two 32 mg tablets for oral suspension is similar to that of one 62.5 mg tablet, and four 32 mg tablets for oral suspension is similar to that of one 125 mg tablet. Because administering two or four 32 mg tablets in adult patients will yield similar systemic exposure, our concern for prescribing the proposed tablets for oral suspension for adult patients is alleviated.

We also note the products differ in strength (32 mg vs. 62.5 mg and 125 mg) and dosage form (tablets for oral suspension vs. tablets). However, it is common and accepted practice to have a product line with multiple dosage forms managed under a shared proprietary name, and while the strengths and dosage forms are different, these differences can be managed with labels and labeling.

Given the aforementioned reasons, and the absence of any postmarketing cases of name confusion with the name, Tracleer, our evaluation finds the use of the same proprietary name, Tracleer, for the proposed tablets for oral suspension is acceptable.

2.2.4 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on August 4, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Cardiovascular and Renal Products (DCRP) on August 10, 2017, they stated no additional concerns with the proposed proprietary name, Tracleer.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Darrel Lyons, OSE project manager, at 301-796-4092.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your July 14, 2017 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. ***Electronic Drug Registration and Listing System (eDRLS) database***

The electronic Drug Registration and Listing System (eDRLS) was established to supports the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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. [b]

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

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

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

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 I: Names identified in the eDRLS database not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name
1.	Aesculus e cort. 32 Special Order
2.	ATACAND
3.	Budesonide
4.	Budesonide Nasal
5.	Candesartan
6.	Candesartan Cilexetil
7.	Childrens RHINOCORT Allergy
8.	EXALGO
9.	Hydromorphone Hydrochloride
10.	incontinence care wipe
11.	Inflammation OTC
12.	Medrol
13.	Methylprednisolone
14.	Neutrogena Shine Control Makeup
15.	Norepinephrine Bitartrate
16.	Ondansetron hydrochloride and dextrose
17.	PremierPro Flushable Wipes with Dimethicone
18.	RHINOCORT Allergy
19.	RHINOCORT AQUA

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/s/

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08/16/2017

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