CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213491Orig1s000

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:	October 7, 2019
Application Type and Number:	NDA 213491
Product Name and Strength:	Procysbi (cysteamine bitartrate) delayed-release oral granules, 75 mg and 300mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Horizon Therapeutics PLC (Horizon)
Panorama #:	2019-33119533
DMEPA Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA Team Leader:	Idalia E. Rychlik, Pharm.D.

Contents

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Procysbi delayed-release capsule was approved on April 30, 2013, under NDA 203389. Horizon submitted the name, Procysbi, for the proposed new dosage form of delayed-release oral granules in packets for review under NDA 213491 on May 16, 2019.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submissions received on July 12, 2019 and September 4, 2019, and prescribing information (PI) received on May 16, 2019.

Table 1. Relevant Product Information for Procysbi		
Product Name	Procysbi (NDA 203389)[a]	Procysbi (NDA 213491)
Intended Pronunciation	\proe sis' bee\	
Initial Approval Date	April 30, 2013	N/A
Active Ingredient	cysteamine bitartrate	
Indication	Procysbi is indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.	
Route of administration	oral	
Dosage Form	delayed-release capsules	delayed release oral granules
Strengths	25 mg and 75 mg	75 mg and 300 mg
Dose and Frequency	<u>Starting and Maintenance Dosing in Cysteamine-Naïve Patients:</u> Start treatment with a dosage equal to $^1/_6$ to ¼ of the maintenance dosage. The maintenance dosage after initial dose escalation is 1.3 g/m^2 of body surface area per day divided into two doses given every 12 hours. Table 1 shows the recommended	

[a] Procysbi. [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. May 2019. [cited 2019 September 27]. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/203389s022lbl.pdf.

<table>
<tr><th colspan="3">Table 1. Relevant Product Information for Procysbi</th></tr>
<tr><th>Product Name</th><th>Procysbi (NDA 203389)[a]</th><th>Procysbi (NDA 213491)</th></tr>
<tr><td></td><td colspan="2">starting and maintenance dosages of PROCYSBI, converted from body-surface area to body weight.

Patients 1 year to less than 6 years: Increase the dosage in 10% increments to the maintenance dosage, while monitoring WBC cystine concentrations. Allow a minimum of 2 weeks between dosage adjustments. If a patient achieves the therapeutic target WBC cystine concentration at a dosage below the recommended weight-based maintenance dosage, then stop dosage escalation and use the dosage as the patient's maintenance dosage.

Patients 6 years of age and older: Gradually increase the dosage over 4 to 6 weeks until the maintenance dosage is achieved.

If a patient experiences initial intolerance, temporarily discontinue PROCYSBI and then re-start at a lower dosage and gradually increase dosage.

Table 1: Starting and Maintenance Dosage of PROCYSBI by Body Weight in Cysteamine-Naïve Patients 1 Year of Age and Older (Dosage Rounded Using Available Capsule or Oral Granules in Packet Strengths)
<table>
<tr><th rowspan="2">Weight in kilograms</th><th colspan="2">Starting PROCYSBI Dosage in mg every 12 hours, as a Fraction of the Maintenance Dosage</th><th rowspan="2">Maintenance PROCYSBI Dosage in mg every 12 hours*</th></tr>
<tr><th>1/6 of dosage</th><th>1/4 of dosage</th></tr>
<tr><td>5 or less</td><td>25</td><td>50</td><td>200</td></tr>
<tr><td>6 to 10</td><td>50</td><td>75</td><td>300</td></tr>
<tr><td>11 to 15</td><td>75</td><td>100</td><td>400</td></tr>
<tr><td>16 to 20</td><td>100</td><td>125</td><td>500</td></tr>
<tr><td>21 to 25</td><td>100</td><td>150</td><td>600</td></tr>
<tr><td>26 to 30</td><td>125</td><td>175</td><td>700</td></tr>
<tr><td>31 to 40</td><td>125</td><td>200</td><td>800</td></tr>
<tr><td>41 to 50</td><td>150</td><td>225</td><td>900</td></tr>
<tr><td>51 kg and greater</td><td>175</td><td>250</td><td>1000</td></tr>
</table>
</td></tr>
</table>

Table 1. Relevant Product Information for Procysbi		
Product Name	Procysbi (NDA 203389)[a]	Procysbi (NDA 213491)
	* Higher dosages may be required to achieve target therapeutic WBC cystine concentration. <u>Switching Patients from Immediate-Release Cysteamine Bitartrate:</u> When switching patients from immediate-release cysteamine bitartrate to PROCYSBI, the starting total daily dose of PROCYSBI is equal to the previous total daily dose of immediate-release cysteamine bitartrate. Divide the total daily dose by two and administer every 12 hours. For patients who may experience temporary intolerance upon starting PROCYSBI, decrease the dosage and then gradually increase to the maintenance dosage. Measure the WBC cystine concentration two weeks after initiation of PROCYSBI. Adjust the PROCYSBI dosage as needed to achieve the therapeutic target WBC cystine concentration. The maximum dosage of PROCYSBI is 1.95 grams/m^2 per day.	
How Supplied	Procysbi delayed-release capsules 25 mg is supplied as bottle of 60 capsules. Procysbi delayed-release capsules 75 mg is supplied as bottle of 250 capsules.	Procysbi delayed-release oral granules (75 mg and 300 mg) are supplied as 60 packets or 120 packets in a carton.
Storage	(b) (4) Dispense (b) (4) in original packaging. Do not subdivide or repackage.	

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Procysbi would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Gastroenterology and Inborn Errors Products (DGIEP) concurred with the findings of OPDP's assessment for Procysbi.

2.2 SAFETY ASSESSMENT

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

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

Horizon did not provide a derivation or intended meaning for the proposed proprietary name, Procysbi, 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 24, 2019 e-mail, the Division of Gastroenterology and Inborn Errors Products (DGIEP) did not forward any comments or concerns relating to Procysbi at the initial phase of the review.

2.2.4 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 Procysbi that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	September 27, 2019
Drug Name	Procysbi [product name]
Event (MedDRA Terms)	DMEPA Official PNR Name Confusion Search Terms Event List
Date Limits	April 30, 2013 to September 1, 2019

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

The search yielded no relevant cases of name confusion with the proprietary name, Procysbi.

[b] USAN stem search conducted on September 27, 2019.

2.2.5 Safety Analysis of Multiple Dose Forms Under the Same Proprietary Name

Procysbi delayed-release capsules was approved on April 30, 2013 and is currently marketed in strengths of 25 mg and 75 mg under NDA 203389. The approved weight-based dosing for the capsules ranges from 25 mg (starting dose) to up to 1,000 mg (maintenance dose) every 12 hours. Under NDA 213491, Horizon proposes a new dosage form, delayed-release oral granules packets, in strengths of 75 mg and 300 mg, to be marketed under the same proprietary name, Procysbi. Procysbi delayed-release oral granules are intended for patients with a gastrostomy tube or for patients who currently administer the contents of capsules with food or liquid. Based on the typical weight-based dosing of the capsules, the oral granule dosage strengths of 75 mg and 300 mg were developed, as compared to the capsules available at strengths of 25 mg and 75 mg. Per the applicant, the 300 mg strength provides more convenience for patients requiring higher dosages, as less packets are needed to achieve the required dose.[c]

We considered the appropriateness of using the proprietary name, Procysbi, for the oral granule formulation proposed under NDA 213491, which would represent a product line extension. We note that the Procysbi capsules and the proposed oral granules share the same active ingredient, indication, route of administration, dose and frequency of administration. Additionally, per the applicant, the proposed granules in the packets are the same granules as those contained in the currently marketed Procysbi delayed-release capsules, which are approved to be swallowed whole or opened to administer the contents of capsules. Per the applicant, the granule formulation is bioequivalent to the currently approved capsule formulation and the recommended dosage and frequency is the same for both dosage forms.

It is common and accepted practice to have a product line with multiple dosage forms share one proprietary name and, while we note the dosage forms are different, these differences can be managed via labeling. We note that both dosage forms have a shared strength (75 mg); however, provided that the review team confirms that these products are bioequivalent, can be substituted on a mg per mg basis, and have no clinically significant differences, we do not anticipate this product line extension will introduce medication errors related to switching between these dosage forms.

Furthermore, we have not retrieved any medication error name confusion reports involving Procysbi. Therefore, given the precedent for using a single proprietary name to market multiple dosage forms, we have no safety concerns with the proposal to market the granules with the proprietary name, Procysbi.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Gastroenterology and Inborn Errors Products (DGIEP) via e-mail on October 4, 2019. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the

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[c] 2.3.1 Introduction to Quality Overall Summary. Lake Forest (IL): Horizon Therapeutics PLC. 2019 May 16. Available from: \\cdsesub1\evsprod\nda213491\0001\m2\23-qos\introduction-granules.pdf

Division of Gastroenterology and Inborn Errors Products (DGIEP) on October 4, 2019, they stated no additional concerns with the proposed proprietary name, Procysbi.

3 CONCLUSION

The proposed proprietary name, Procysbi, is acceptable.

If you have any questions or need clarifications, please contact Alvis Dunson, OSE project manager, at 301-796-6400.

3.1 COMMENTS TO HORIZON THERAPEUTICS PLC

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

If any of the proposed product characteristics as stated in your submissions, received on July 12, 2019 and September 4, 2019, 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.

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.

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/s/

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