



Horizon Therapeutics plc Announces Availability of PROCYSBI® (Cysteamine Bitartrate) Delayed-Release Oral Granules in Packets in the United States

-- New dosage form in tear-open packets provides a convenient option for people living with cystinosis --

DUBLIN — April 27, 2020 — Horizon Therapeutics plc (Nasdaq: HZNP) announced today that PROCYSBI® (cysteamine bitartrate) delayed-release oral granules in packets are now available in the United States and can be ordered in 75 mg and 300 mg dosage strengths for adults and children one year of age and older living with nephropathic cystinosis. The U.S. Food and Drug Administration (FDA) approved this new dosage form in February 2020.

In the United States, PROCYSBI is now available in two forms: tear-open packets and capsules. Both forms contain the same PROCYSBI granules, also called microbeads, that provide 12 hours of cystine control. PROCYSBI capsules will continue to be available in 25 mg and 75 mg dosage strengths.

The new tear-open packets offer a convenient option for cystinosis patients who may have difficulty swallowing, need to sprinkle the granules on certain foods or mix with select liquids, or administer medication through a gastrostomy tube (G-tube). Additionally, the ability to access PROCYSBI granules in tear-open packets may help reduce the burden families living with cystinosis often face with managing multiple medications every day.

“This is a very helpful step forward in directly meeting the needs of patients and families in the cystinosis community,” said Paul Grimm, M.D., pediatric nephrologist and professor of pediatrics (nephrology) at The Lucile Salter Packard Children's Hospital. “Physicians now have the option of prescribing tear-open packets for any of their patients who have had to open individual capsules to remove the granules. The day-to-day challenges of managing a rare disease like cystinosis can be overwhelming, so new developments like this one can make an important difference in the lives of families living with cystinosis.”

The coating of PROCYSBI granules in tear-open packets and inside the capsules is designed to break down in low acid environments. Thus, the same steps that are required when taking the capsules with food are also required when taking the oral granules in tear-open packets. The packets must be opened and mixed with select high acidity foods or liquids identified in the full prescribing information. It is important to take either form of PROCYSBI with high acidic/low-fat foods and to avoid high-fat foods (such as avocados, cheese and nuts) right before and after taking PROCYSBI.

“Input and feedback from families and health professionals in the cystinosis community helped guide the development of the oral granules in tear-open packets,” said Gregg Checani, M.D., executive medical director, medical affairs and clinical science, Horizon. “By meeting with the community and learning from them throughout the year, we are able to develop solutions for patients and families based on their needs.”



About Nephropathic Cystinosis

Nephropathic cystinosis is a rare, life-threatening metabolic lysosomal storage disorder that causes toxic accumulation of cystine in all cells, tissues and organs in the body. If untreated, elevated cystine accumulation leads to progressive, irreversible tissue damage and multi-organ failure, including kidney failure, blindness, muscle wasting and premature death. It is estimated that only about 2,000 people worldwide are currently diagnosed with nephropathic cystinosis. Nephropathic or “classic infantile” cystinosis – the most common and most severe form of the disease – is typically diagnosed in infancy and requires lifelong cystine depleting therapy.¹

About PROCYSBI

PROCYSBI (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules is a cystine-depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Patients with serious hypersensitivity reaction, including anaphylaxis to penicillamine or cysteamine.

WARNINGS AND PRECAUTIONS

- **Ehlers-Danlos-like Syndrome:** Skin and bone lesions that resemble clinical findings for Ehlers-Danlos-like syndrome have been reported in patients treated with high doses of immediate-release cysteamine bitartrate or other cysteamine salts. Monitor patients for development of skin or bone lesions and reduce PROCYSBI dosing if patients develop these lesions.
- **Skin Rash:** Severe skin rashes such as erythema multiforme bullosa or toxic epidermal necrolysis have been reported in patients receiving immediate-release cysteamine bitartrate. Discontinue use if severe skin rash occurs.
- **Gastrointestinal (GI) Ulcers and Bleeding:** GI ulceration and bleeding have been reported in patients receiving immediate-release cysteamine bitartrate. Monitor for GI symptoms and consider decreasing the dose if severe symptoms occur.
- **Central Nervous System (CNS) Symptoms:** CNS symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy have been associated with immediate-release cysteamine. Monitor for CNS symptoms; interrupt or reduce the dose for severe symptoms or those that persist or progress.
- **Leukopenia and/or Elevated Alkaline Phosphatase Levels:** Cysteamine has been associated with reversible leukopenia and elevated alkaline phosphatase levels. Monitor white blood cell counts and alkaline phosphatase levels; decrease or discontinue the dose until values revert to normal.
- **Benign Intracranial Hypertension:** Benign intracranial hypertension (pseudotumor cerebri; PTC) and/or papilledema has been reported in patients receiving immediate-release cysteamine bitartrate treatment. Monitor for signs and symptoms of PTC; interrupt or reduce the dose for signs/symptoms that persist, or discontinue if diagnosis is confirmed.



ADVERSE REACTIONS

The most common adverse reactions reported in PROCYSBI clinical trials ($\geq 5\%$): were:

- *Patients 2 years of age and older previously treated with cysteamine:* vomiting, nausea, abdominal pain, headache, conjunctivitis, influenza, gastroenteritis, nasopharyngitis, dehydration, ear infection, upper respiratory tract infection, fatigue, arthralgia, cough, and pain in extremity.
- *Patients 1 year of age and older naïve to cysteamine treatment:* vomiting, gastroenteritis/viral gastroenteritis, diarrhea, breath odor, nausea, electrolyte imbalance, headache.

DRUG INTERACTIONS

- Drugs that increase gastric pH may alter the pharmacokinetics of cysteamine due to the premature release of cysteamine from PROCYSBI and increase WBC cystine concentration. Monitor WBC cystine concentration with concomitant use.
- Consumption of alcohol with PROCYSBI may increase the rate of cysteamine release and/or adversely alter the pharmacokinetic properties, as well as the effectiveness and safety of PROCYSBI.
- PROCYSBI can be administered with electrolyte (except bicarbonate) and mineral replacements necessary for management of Fanconi Syndrome as well as vitamin D and thyroid hormone.

USE IN SPECIFIC POPULATIONS

- *Lactation:* Because of the potential risk for serious adverse reactions in breastfed children from cysteamine, breastfeeding is not recommended during treatment with PROCYSBI.

Please see [Full Prescribing Information](#).

About Horizon

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare and rheumatic diseases. Our pipeline is purposeful: we apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives. For more information on how we go to incredible lengths to impact lives, please visit www.horizontherapeutics.com and follow us on [Twitter](#), [LinkedIn](#), [Instagram](#) and [Facebook](#).

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential benefits of availability of PROCYSBI® (cysteamine bitartrate) delayed-release oral granules in packets. These forward-looking statements are based on management expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward-looking statements as a result of various factors. These factors include Horizon's ability to successfully launch and market PROCYSBI® (cysteamine bitartrate) delayed-release oral granules in packets and the availability of reimbursement and payor coverage, as well as those described in Horizon's filings with the



United States Securities and Exchange Commission, including those factors discussed under the caption "Risk Factors" in those filings. Forward-looking statements speak only as of the date of this press release and Horizon does not undertake any obligation to update or revise these statements, except as may be required by law.

References

1. <https://ghr.nlm.nih.gov/condition/cystinosis>. Accessed July 16, 2019.

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