



Horizon Pharma plc Announces FDA Approval to Expand the Indication for PROCYSBI® (cysteamine bitartrate) Delayed-Release Capsules to Include Children One Year of Age and Older Living with Nephropathic Cystinosis

December 27, 2017

DUBLIN, Ireland, Dec. 27, 2017 (GLOBE NEWSWIRE) -- Horizon Pharma plc (NASDAQ:HZNP) today announced the U.S. Food and Drug Administration (FDA) has approved an expansion to the indication for PROCYSBI® (cysteamine bitartrate) delayed-release capsules to include children one year of age and older living with nephropathic cystinosis. With this update to the indication, the PROCYSBI prescribing information now includes revised guidance for physicians administering the medicine to pediatric patients, including new clinical evidence and dosing information for very young children. PROCYSBI was previously FDA-approved for adults and children as young as two years of age.

"Data included in the updated label provide further evidence around the unique role of PROCYSBI in helping physicians manage young children during one of the most crucial periods for growth," said Craig B. Langman, M.D., lead investigator for the study that led to the label update, head of kidney diseases and the Isaac A. Abt MD professor of kidney diseases, The Ann and Robert H. Lurie Children's Hospital of Chicago, as well as professor of pediatrics at Northwestern University Feinberg School of Medicine. "As a physician who conducts research and also cares for kids with nephropathic cystinosis, I'm particularly excited about the outcome of the clinical study and the subsequent PROCYSBI labeling update."

The PROCYSBI labeling was updated based on a long-term, prospective, open-label study that enrolled 17 people living with nephropathic cystinosis, including 15 children between the ages of 1 and 5 years old, who had not previously been treated with cysteamine therapy. Children enrolled in the study experienced lowering of white blood cell (WBC) cystine levels from poor controlled to well controlled at 12 and 18 month measurements. WBC levels are the biomarker for disease control. Additionally, they experienced measured improvements in growth milestones including weight and height. The most common adverse reactions (>10%) in patients treated in clinical trials reflected in the FDA approved product labeling were vomiting, gastroenteritis/viral gastroenteritis, diarrhea, breath odor, nausea, electrolyte imbalance and headache. This study was required by the FDA as a post-marketing commitment after PROCYSBI was approved.

"The expanded PROCYSBI indication and revised prescribing information provide important guidance for physicians caring for people living with nephropathic cystinosis, particularly those treating very young children," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "We are grateful for the families who enrolled their children in the clinical study that resulted in this update to the prescribing information – their participation led to the availability of new data that may improve the treatment of children living with nephropathic cystinosis."

About 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

IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE: PROCYSBI® (cysteamine bitartrate) delayed-release capsules is a cystine-depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.

CONTRAINDICATIONS:

- Hypersensitivity 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.
 - These include molluscoid pseudotumors (purplish hemorrhagic lesions), skin striae, bone lesions (including osteopenia, compression fractures, scoliosis and genu valgum), leg pain and joint hyperextension.
 - One patient on immediate-release cysteamine bitartrate with serious skin lesions subsequently died of acute cerebral ischemia with marked vasculopathy.
 - Patients should be monitored for development of skin or bone lesions and PROCYSBI dosing should be interrupted if patients develop these lesions. PROCYSBI may be restarted at a lower dose under close supervision, then slowly increased to the appropriate therapeutic dose.
- **Skin Rash:** Severe skin rashes such as erythema multiforme bullosa or toxic epidermal necrolysis have been reported in patients receiving immediate-release cysteamine bitartrate. If severe skin rashes develop, use of PROCYSBI should be permanently discontinued.

- **Gastrointestinal Ulcers and Bleeding:** Gastrointestinal (GI) ulceration and bleeding have been reported in patients receiving immediate-release cysteamine bitartrate.
 - GI tract symptoms including nausea, vomiting, anorexia and abdominal pain, sometimes severe, have been associated with cysteamine. If severe GI tract symptoms develop, decreasing the dose of PROCYSBI should be considered.
- **Central Nervous System Symptoms:** Central Nervous System (CNS) symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy have been associated with immediate-release cysteamine.
 - Neurological complications have also been described in some patients with cystinosis who have not been treated with cysteamine.
 - Patients who develop CNS symptoms should be carefully evaluated and monitored. Medication should be interrupted or the dose should be adjusted as necessary for patients with severe symptoms or with symptoms that persist or progress.
 - PROCYSBI may impair the ability of patients to perform tasks such as driving or operating machinery.
- **Leukopenia and/or Elevated Alkaline Phosphatase Levels:** Cysteamine has been associated with reversible leukopenia and elevated alkaline phosphatase levels. White blood cell counts and alkaline phosphatase levels should be monitored. If test values remain elevated, consider decreasing the dose or discontinuing the drug 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.
 - Patients should be monitored for signs and symptoms of PTC, including headache, tinnitus, dizziness, nausea, diplopia, blurry vision, loss of vision, pain behind the eye or pain with eye movement. If signs/symptoms persist, dosing should be interrupted or the dose should be decreased and the patient should be referred to an ophthalmologist. If the diagnosis is confirmed, use of PROCYSBI should be permanently discontinued.

ADVERSE REACTIONS:

The most common adverse reactions (>10%) in patients treated in clinical trials reflected in the FDA approved product labeling were vomiting, gastroenteritis/viral gastroenteritis, diarrhea, breath odor, nausea, electrolyte imbalance and headache.

To report SUSPECTED ADVERSE REACTIONS, contact Horizon Pharma USA, Inc, at 1-855-888-4004 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS:

- **Drugs that Increase Gastric pH:** PROCYSBI should be administered at least 1 hour before or 1 hour after medications containing bicarbonate or carbonate.
- 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:

- Breastfeeding is not recommended while taking PROCYSBI.

Pediatric Use:

- The safety and effectiveness of PROCYSBI have been established in pediatric patients 1 year of age and older for the treatment of nephropathic cystinosis. The safety profile in pediatric patients was similar to adults.
- The safety and effectiveness of PROCYSBI have not been established in patients less than 1 year of age.

Horizon Pharma plc

Horizon Pharma plc is a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. The Company markets 11 medicines through its orphan, rheumatology and primary care business units. For more information, please visit www.horizonpharma.com. Follow [@HZNPplc](https://twitter.com/HZNPplc) on Twitter, like us on [Facebook](https://www.facebook.com/HorizonPharma) or view careers on our [LinkedIn](https://www.linkedin.com/company/horizon-pharma) page.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential of PROCYSBI to treat patients with nephropathic cystinosis and the impact of the label expansion and additional pediatric data. 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 whether patients are willing to use PROCYSBI to treat nephropathic cystinosis and whether use of PROCYSBI outside of the clinical trial setting will demonstrate results consistent with clinical trials, as well as those factors described in Horizon Pharma'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 Pharma does not undertake any obligation to update or revise these statements, except as may be required by law.

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References:

1. Cystinosis Research Foundation. "About cystinosis." Available at <http://www.cystinosisresearch.org/About-Cystinosis/>. Accessed Nov. 2, 2017.

 [Primary Logo](#)

Source: Horizon Pharma plc