PROCYSBI® (CYSTEAMINE BITARTRATE) DELAYED-RELEASE CAPSULES AND DELAYED-RELEASE ORAL GRANULES PATIENT ENROLLMENT FORM INSTRUCTIONS

The Patient Enrollment Form is required to initiate treatment with Horizon Therapeutics' prescription medicine, PROCYSBI.

Instructions:

1. Fill out all patient information, including the most recent results of a white blood cell (WBC) cystine level test, recent history with CYSTAGON® (cysteamine bitartrate) capsules, and use of a gastrostomy tube (G-tube).
2. Fill out all required prescriber information, including all contact information for the practice or facility.
3. Complete and/or review all required insurance information for the patient and, if possible, attach copies of the patient's insurance cards for primary as well as supplementary insurance.
4. Complete the prescription and clinical information in its entirety; all fields are required. Reference the included select PROCYSBI dosing instructions or the PROCYSBI Full Prescribing Information for complete dosing information.
5. Review, sign, and date the prescriber certification at the bottom of the Patient Enrollment Form. In signing, you are indicating to dispense PROCYSBI as written. If a substitution is allowed, it should be noted.
6. Check with your patient to ensure he or she has printed, signed, and dated the required Patient Authorization Form providing HIPAA authorization for Horizon By Your Side, a patient support program, and initiation of patient support.
7. Fax pages 1 and 2 of this form, along with both sides of the patient's medical and prescription drug benefit cards, to the Horizon By Your Side team at 1-877-773-9411, or email them to PROHBYS@horizontherapeutics.com. Retain a copy of this form in the patient's records.

Please see complete IMPORTANT SAFETY INFORMATION on last page and click here for the PROCYSBI Full Prescribing Information.

PROCYSBI® (CYSTEAMINE BITARTRATE) DELAYED-RELEASE CAPSULES AND DELAYED-RELEASE ORAL GRANULES PATIENT ENROLLMENT FORM

Please fax completed form to 1-877-773-9411, or email it to PROHBYS@horizontherapeutics.com.

HORIZON
Phone: 1-855-888-4004
Fax: 1-877-773-9411
PROCYSBI.com

1. PATIENT INFORMATION

First Name _____ MI _____ Last Name _____

Address _____ City _____ State ☐ Zip _____

Home Phone _____ Mobile Phone _____

Date of Birth _____ Gender ☐ M ☐ F Height _____ Weight _____

Email _____ Preferred Method of Contact ☐ Home ☐ Mobile ☐ Email ☐ Mail

Currently taking CYSTAGON® (cysteamine bitartrate)? ☐ Yes ☐ No

Last CYSTAGON daily dose (mg/day) _____

Currently on dialysis? ☐ Yes ☐ No

Does the patient have a G-tube (feeding tube)? ☐ Yes ☐ No

White blood cell (WBC) test in the last year? ☐ Yes ☐ No

(A bolus [straight] feeding tube 14 French or larger is recommended.)

ALTERNATIVE CONTACT AND/OR CAREGIVER

First Name _____ Last Name _____ Home Phone _____

Mobile Phone _____ Email _____ Preferred Method of Contact ☐ Home ☐ Mobile ☐ Email

2. PRESCRIBER INFORMATION

Preferred Method of Contact ☐ Email ☐ Phone

Prescriber First Name _____ MI _____ Last Name _____ Prescriber NPI# _____

Address _____ City _____ State ☐ Zip _____

Phone _____ Fax _____ Physician Specialty _____

Office Contact Name _____ Email _____ Phone _____

3. INSURANCE INFORMATION — Please attach a copy of both sides of the patient's insurance card(s).

☐ No Insurance

PRIMARY INSURANCE

Insurance Carrier _____

Customer Service Phone _____

Subscriber Name _____

Patient's Relationship to Subscriber _____

Subscriber Date of Birth _____

Subscriber ID Number _____

Policy/Employer/Group Number _____

SECONDARY INSURANCE (if any)

Insurance Carrier _____

Customer Service Phone _____

Subscriber Name _____

Patient's Relationship to Subscriber _____

Subscriber Date of Birth _____

Subscriber ID Number _____

Policy/Employer/Group Number _____

Prescription Card? ☐ Yes If Yes, Carrier: _____ Phone _____

4. PRESCRIPTION AND CLINICAL INFORMATION

Diagnosis (ICD-10-CM Code) ☐ E72.04 ☐ Other _____

Drug Name: ☐ PROCYSBI Capsules: ☐ 25 mg _____ Quantity and/or ☐ 75 mg _____ Quantity

Directions: _____ mg Prescribed Total Daily Dose

_____ Days' Supply _____ Refills

Drug Name: ☐ PROCYSBI Granule Packets: ☐ 75 mg _____ Quantity and/or ☐ 300 mg _____ Quantity

Directions: _____ mg Prescribed Total Daily Dose

_____ Days' Supply _____ Refills

eg, Capsules: 600 mg q12h or 500 mg (6 x 75 mg capsules + 2 x 25 mg capsules) q12h. Packets: 600 mg q12h or 525 mg (1 x 300 mg packets + 3 x 75 mg packets) q12h.

Dose Titration, see PROCYSBI Dosing Information for Healthcare Prescribers on page 3 for more information.

Note: The prescriber is to comply with his/her state-specific prescription requirements such as e-prescribing, state-specific prescription form, fax language, etc.

Is the patient allergic to penicillamine, cysteamine, or any other medication? If yes, please list: _____

Prescriber Certification

I certify that the above therapy is medically necessary, that the information provided is accurate to the best of my knowledge and that my patient is being administered PROCYSBI in accordance with the labeled use of the product. I understand that Horizon Therapeutics USA, Inc. and its affiliates and their respective employees or agents (collectively, "Horizon") will use this information to administer the Horizon By Your Side program (the "Program"), which provides a wide array of patient-focused services, including providing logistical and non-medical treatment support for PROCYSBI, as prescribed, and educating about the insurance process. By my signature, I also certify that (1) my patient or his/her personal representative has provided a signed HIPAA authorization that allows me to share protected health information with Horizon for purposes of the Program and (2) I have obtained the patient's authorization to release such information as may be required for Accredo Health Group, Inc. (or another party acting on behalf of Horizon) to assess insurance coverage for PROCYSBI and assistance in initiating or continuing PROCYSBI as prescribed. I further understand and agree that (a) any medication or service provided through the Program as a result of this form is for the named patient only and is not being made in exchange for any express or implied agreement or understanding that I would recommend, prescribe, or use PROCYSBI or any other Horizon product or service, for any other person; (b) my decision to prescribe PROCYSBI was based solely on my professional determination of medical necessity; and (c) I will not seek reimbursement for any medication or service provided by or through the Program from any government program or third-party insurer. I understand that Horizon may modify or terminate the Program at any time without notice. The completion and submission of coverage- or reimbursement-related documentation are the responsibility of the patient and healthcare provider. Horizon makes no representation or guarantee concerning coverage or reimbursement for any item or service.

State requirements: The prescriber is to comply with his/her state-specific prescription requirements such as e-prescribing, state-specific prescription form, fax language, etc. Noncompliance with state-specific requirements could result in outreach to the prescriber.

By filling out and signing this form, the enrollment process in Horizon By Your Side has initiated; however, your patient must sign a Patient Authorization to complete enrollment in Horizon By Your Side. Please note that your patient will not benefit from the services and support offered by Horizon By Your Side unless your patient signs a Patient Authorization, consenting to receiving such services. If your patient does not sign the Patient Authorization contained within this form, Horizon will contact the patient to determine whether the patient is interested in signing a separate Patient Authorization.

X Prescriber Signature _____ Date _____

Written signature only; stamps not acceptable.

(Dispense as Written) _____ (Substitution Permitted)

Please see complete IMPORTANT SAFETY INFORMATION on last page and click here for the PROCYSBI Full Prescribing Information.

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PROCYSBI.com

Patient Consent for Patient Information, Enrolling in Services, and Accessing Financial Support (Referred to as "Patient Authorization")

I hereby authorize my healthcare providers, my health insurance carriers, and my pharmacies to use and disclose my individually identifiable health information, including my medical records, insurance coverage information, and my name, address and telephone number to Horizon Therapeutics USA, Inc. and its affiliates and their respective agents and representatives (collectively, "Horizon"), including third parties authorized by Horizon to administer drug support and to dispense drugs (collectively, "Horizon By Your Side") for the following purposes: (1) to establish eligibility for benefits; (2) to communicate with my healthcare providers and me about my treatment or condition and related products; (3) to facilitate the provision of products, supplies, or services by a third party including, but not limited to, specialty pharmacies; (4) to register me in any applicable product registration program required for my treatment; (5) to enroll me in eligible patient support programs offered by Horizon By Your Side and/or Horizon, including nursing or patient access support services (government-reimbursed programs may not be eligible for all support services offered; please contact Horizon By Your Side for determination); and (6) to send me marketing information or offer me products and services related to my treatment or condition (or other products or services in which I might be interested) and to contact me occasionally to obtain my feedback (for market research purposes only) about my treatment, my condition, or my experience with Horizon and/or Horizon By Your Side otherwise as required or permitted by law. Further, I appoint the Program, on my behalf, to proceed with Program services and to convey this prescription to the dispensing pharmacy, to the extent permitted under state law. I understand the pharmacies may receive a fee from Horizon in exchange for (1) providing me with certain materials and information described above, and (2) using or disclosing certain health information pursuant to this Authorization.

I understand that Horizon, as well as my healthcare providers, cannot require me, as a condition of having access to medications, prescription drugs, treatment, or other care, to sign this Authorization. I understand that I am entitled to a copy of this Authorization.

I understand that information disclosed pursuant to this Authorization in some cases may be redisclosed by the recipient and no longer protected by HIPAA or other privacy laws. But Horizon has agreed to use and disclose my information only for purposes of operating the Program. I understand that I may cancel this Authorization at any time by mailing a signed letter requesting such cancellation to Horizon By Your Side, 1 Horizon Way, Deerfield, IL 60015, but that this cancellation will not apply to any information used or disclosed by my healthcare providers and/or health insurance carriers based on this Authorization before they are notified that I have cancelled it. Unless required by state law, this Authorization is valid for whichever is greater: (a) the duration of remaining on this treatment or (b) 10 years from the date signed below. A photocopy of this Authorization will be treated in the same manner as the original.

Date: _____

Patient's Printed Name: _____

Patient's/Legally Authorized Representative's Signature: _____

Legally Authorized Representative's Printed Name (if required): _____

Patient's/Legally Authorized Representative's Home Address:

Street Address: _____

City: _____ State: _____ Zip Code: _____

Patient's/Legally Authorized Representative's Telephone: _____ ☐ Home ☐ Mobile

Patient's/Legally Authorized Representative's Email Address: _____

Legally Authorized Representative's Relationship to Patient: ☐ Spouse ☐ Parent/Legal Guardian ☐ Representative per Power of Attorney

Is there someone else with whom we may discuss your protected health information? ☐ No ☐ Yes

Name: _____

Name: _____

Relationship to you: _____

HORIZON

PROCYSBI DOSING INFORMATION *FOR HEALTHCARE PRESCRIBERS*

PROCYSBI®
(cysteamine bitartrate) delayed-release capsules delayed-release oral granules

PROCYSBI is available as[1]:	**25 mg: 60 delayed-release capsules/bottle**	**75 mg: 60 delayed-release packets/box**
	75 mg: 250 delayed-release capsules/bottle	**300 mg: 120 delayed-release packets/box**

Patients starting PROCYSBI who are cysteamine naïve[1]

- Initiate cysteamine treatment immediately after diagnosis of nephropathic cystinosis
- Patients should be started on PROCYSBI at a fraction (1/6 to 1/4) of the maintenance dosage and gradually titrated up to the maintenance dosage over 4 to 6 weeks
  - Patients 1 year to less than 6 years: Increase the dosage in 10% increments to the maintenance dosage, while monitoring white blood cell (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
- The maintenance dosage after initial dose escalation is 1.3 g/m^2 of body surface area per day divided into 2 doses given every 12 hours. The table below shows the recommended starting and maintenance dosages of PROCYSBI, converted from body surface area to body weight

Patients converting to PROCYSBI from immediate-release (IR) cysteamine (CYSTAGON)[1]

- When switching patients from IR cysteamine bitartrate to PROCYSBI, the starting total daily dose of PROCYSBI is equal to the previous total daily dose of IR cysteamine bitartrate. Divide the total daily dose by 2 and administer every 12 hours

Starting and Maintenance Dosage of PROCYSBI by Body Weight in Cysteamine-Naïve Patients 1 Year of Age and Older (Dosage Rounded Using Available Capsule and Packet Strengths)

Weight in kg	Starting PROCYSBI Dosage in mg Every 12 Hours, as a Fraction of the Maintenance Dosage		Maintenance PROCYSBI Dosage in mg Every 12 Hours*
	1/6 of dosage	1/4 of dosage	
5 or less	25	50	200
6 to 10	50	75	300
11 to 15	75	100	400
16 to 20	100	125	500
21 to 25	100	150	600
26 to 30	125	175	700
31 to 40	125	200	800
41 to 50	150	225	900
51 and greater	175	250	1000

*Higher dosages may be required to achieve target therapeutic WBC cystine concentration.

Monitoring dosage[1]

- If a patient's precise calculated dosage cannot be obtained, round to the nearest 25 mg for capsules or 75 mg for packets. Only use whole capsules and packets
- After maintenance dosage of PROCYSBI has been achieved, measure the WBC cystine concentration and titrate the PROCYSBI dosage as needed to achieve target WBC cystine concentrations
- If a dosage adjustment is necessary, increase the dosage by 10%. For patients 1 year to less than 6 years of age, allow a minimum of 2 weeks between dose increments. The maximum dosage of PROCYSBI is 1.95 g/m^2 per day

If tolerability issues occur with PROCYSBI[1]

- **If adverse reactions occur, decrease the PROCYSBI dosage and then gradually increase to the maintenance dosage**
- **For cysteamine-naïve patients who have initial intolerance, temporarily discontinue PROCYSBI and then restart at a lower dosage and gradually increase to the maintenance dosage**

Please click here for the Full Prescribing Information for complete dosing and administration instructions.

Adherence to cystine-depleting therapy is critical for optimal cystine control[2,3]

- Patients/caregivers should be urged to take PROCYSBI consistently according to the dosing schedule recommended in the prescribing information[1]

References: 1. PROCYSBI (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules [prescribing information] Horizon. **2.** Gahl WA, Thoene JG, Schneider JA. Cystinosis. *N Engl J Med*. 2002;347(2):111-121. **3.** Brodin-Sartorius A, Tête M-J, Niaudet P, et al. Cysteamine therapy delays the progression of nephropathic cystinosis in late adolescents and adults. *Kidney Int*. 2012;81(2):179-189.

HORIZON

INDICATION and IMPORTANT SAFETY INFORMATION

PROCYSBI®
(cysteamine bitartrate)
delayed-release capsules
delayed-release oral granules

INDICATION

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.
- **Fibrosing Colonopathy:** Fibrosing colonopathy has been reported with postmarketing use of PROCYSBI. Evaluate patients with severe, persistent, and/or worsening abdominal symptoms for fibrosing colonopathy. If the diagnosis is confirmed, permanently discontinue PROCYSBI and switch to immediate-release cysteamine bitartrate capsules.
- **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 *(≥ 5%):* were:

- *Patients 2 years of age and older previously treated with cysteamine:* vomiting, nausea, abdominal pai n, 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.