PROCYSBI delivers continuous cystine control for your patients with dosing every 12 hours, at times that work for them[1]

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.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

CYSTINOSIS IS PROGRESSIVE, BUT CAN BE MANAGED[2,3]

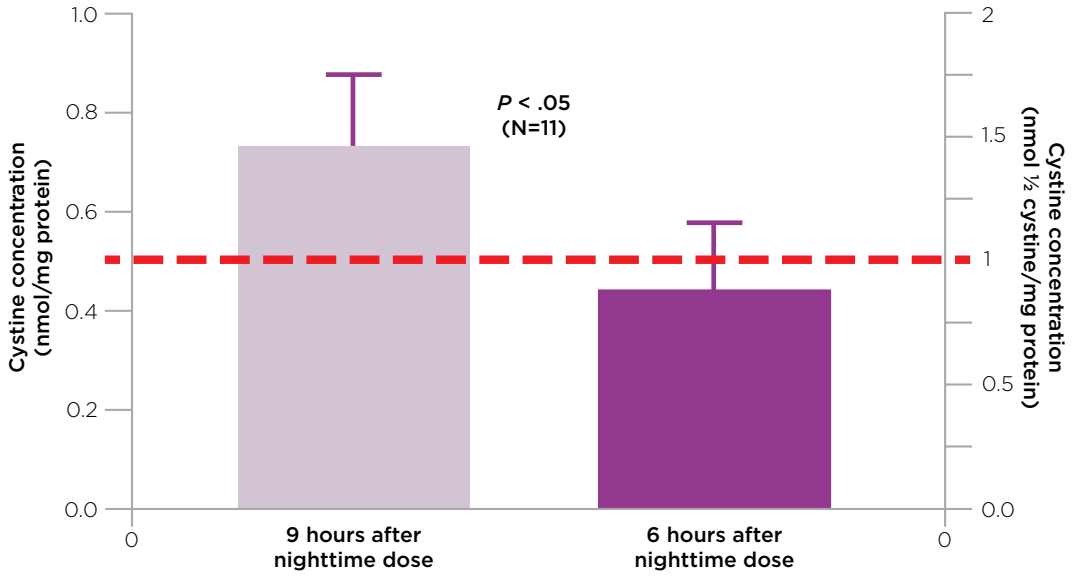
Cystinosis is a progressive, inherited disorder that leads to toxic levels of cystine inside lysosomes[2,4]

- Without treatment, cystine accumulates to toxic levels and causes irreversible damage to the body
- Cystinosis first affects the kidneys, but over time causes damage throughout the body

Cystinosis can be managed by controlling cystine levels with cysteamine, a cystine-depleting therapy (CDT)[2,3]

- CDT is the only way to remove cystine and its crystals from lysosomes throughout the body[2]
- Adherent use of CDT is critical to managing cystinosis, as cystine levels rise quickly[5,6]
- In a study, patients who delayed their dose of CDT by 3 hours (9 hours vs 6 hours) had white blood cell (WBC) cystine levels that were 65% higher and in excess of the target level[6]

Comparison of WBC cystine content with 9-hour vs 6-hour dosing of immediate-release (IR) cysteamine[6]



Target cystine levels below 0.5 nmol cystine/mg protein (=1.0 nmol ½ cystine/mg protein)

Adapted from Levtchenko EN, et al. *Pediatr Nephrol.* 2006.

Comparison of morning leukocyte content with IR CDT when administered every 6 hours (8 AM, 2 PM, 8 PM, 2 AM) vs 4 times a day with a 9-hour night pause (8 AM, 1 PM, 6 PM, 11 PM) in a cohort of 22 Dutch patients (mean age 14.7 ± 9.7 years) with nephropathic cystinosis.[6]

With ongoing and consistent use of CDT, cystine levels may be controlled and some damage to organs may be prevented or limited.[2,4]

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

DOSING EVERY 12 HOURS FOR CONTINUOUS CYSTINE CONTROL[1]

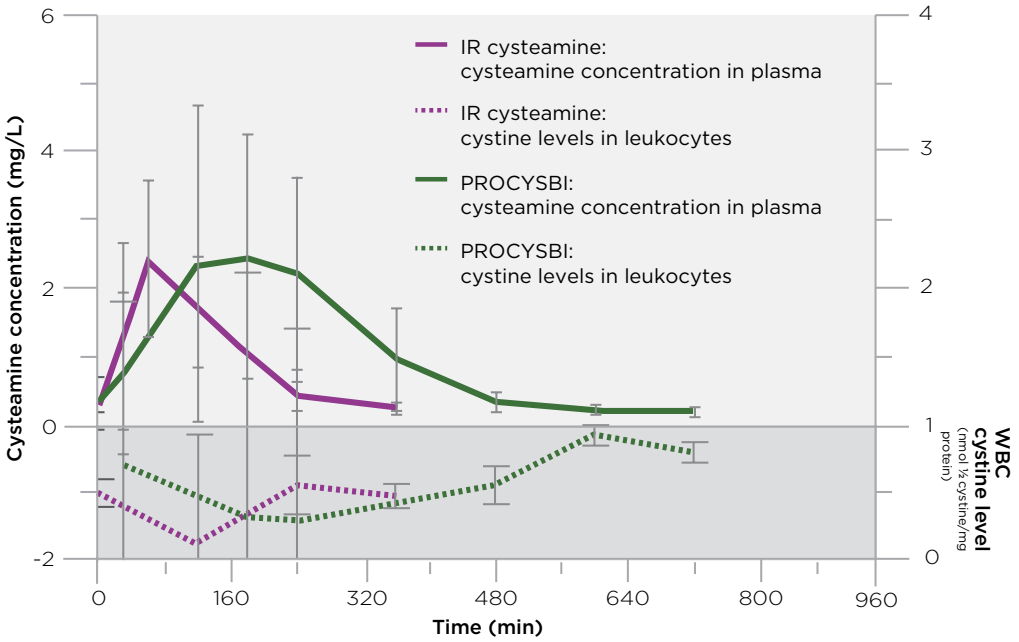
Proprietary delayed-release technology releases cysteamine gradually, providing 12 hours of continuous cystine control[7-10]

- PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules contain microbeads that are absorbed in the alkaline environment of the small intestine[7-10]
- With dosing that continuously controls cystine levels for 12 hours, your patients can find a dosing schedule that works for them[1]

PROCYSBI maintained cystine below target levels over the entire 12-hour dosing period[9]

- In a phase 3 clinical trial, PROCYSBI given every 12 hours was found to be noninferior to IR cysteamine bitartrate given every 6 hours[1]

Plasma cysteamine concentrations and leukocyte cystine levels following a single dose of PROCYSBI vs IR cysteamine (N=38)[9]



Adapted from Langman CB, et al. *Clin J Am Soc Nephrol.* 2012.

Please see the full clinical trial study design for RP103-03 on the flashcard in the pocket of this brochure.

SELECT IMPORTANT SAFETY INFORMATION

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.

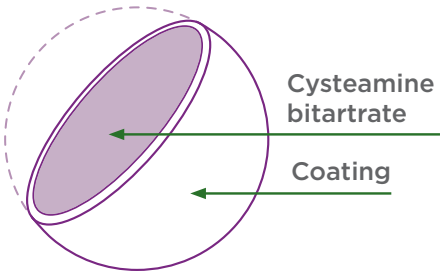
Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

HOW PROCYSBI IS DESIGNED TO WORK

PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules use proprietary technology

PROCYSBI granules, also called "microbeads," are composed of cysteamine bitartrate surrounded by an acid-resistant enteric coating. The microbeads release cysteamine gradually, providing 12 hours of continuous cystine control.[1,7-10]

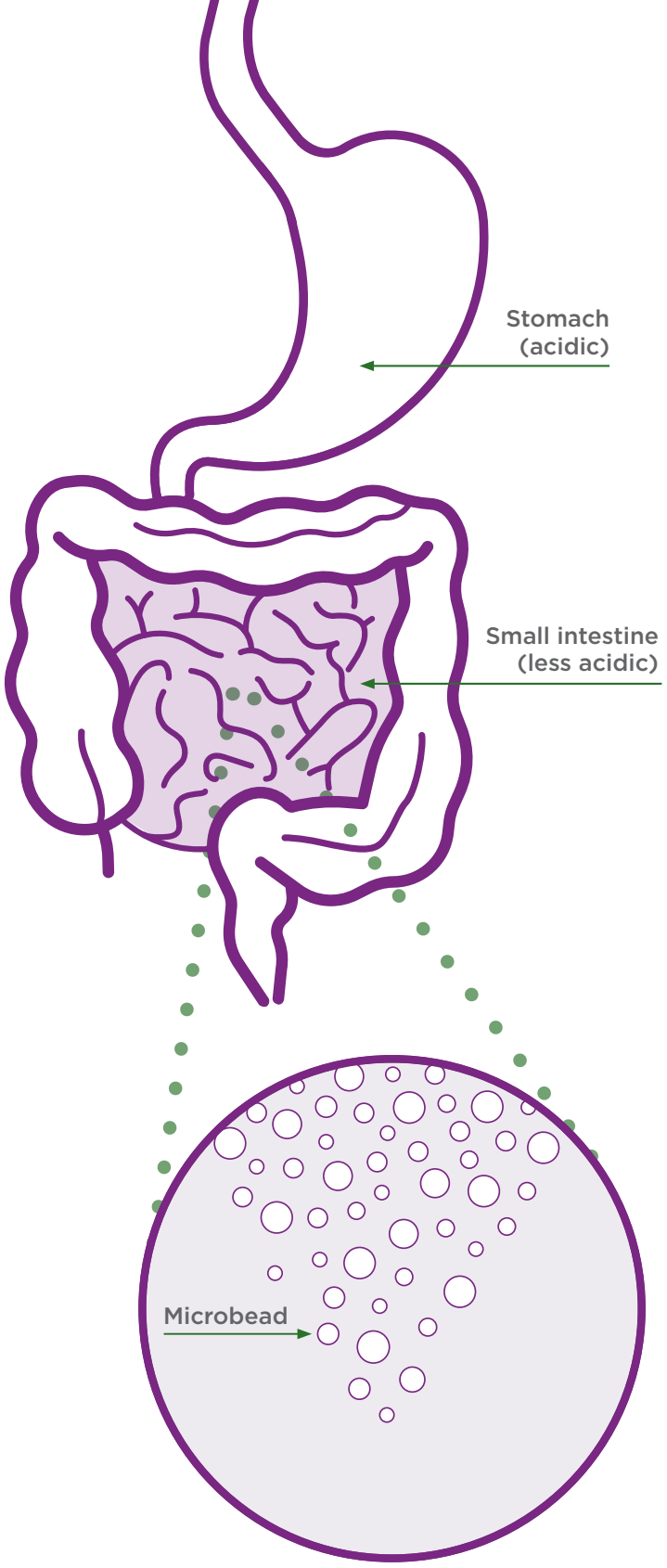


To work properly, PROCYSBI microbeads must dissolve and release cysteamine bitartrate in the small intestine. The coating on the microbeads helps to control where and how medicine is released by allowing the cysteamine bitartrate to pass through the acidic stomach to the alkaline environment of the small intestine.[7-10]

Once in the small intestine, the coating begins to dissolve and the microbeads release cysteamine bitartrate gradually. This allows PROCYSBI to control cystine levels continuously over the dosing interval.[7-10]

PROCYSBI and the stomach

- What a patient eats and drinks can affect acid levels. **If acid levels are too low, it can result in the medicine releasing too soon (in the stomach)**[10]
- Some medicines, including those that contain bicarbonate or carbonate, may change the acid levels in the stomach. **PROCYSBI must be taken 1 hour before or after these medicines**[1]
- **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[1]



Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

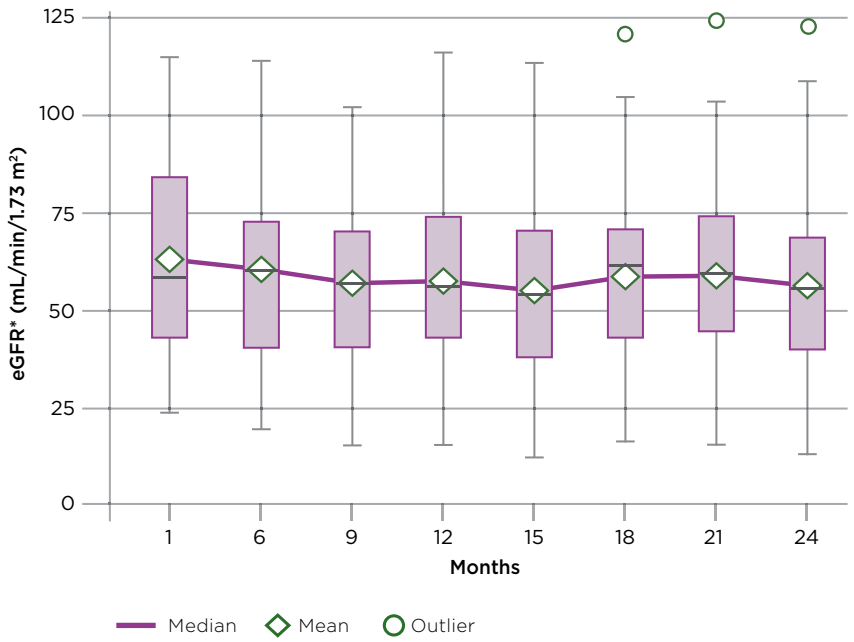
PROCYSBI®
(cysteamine bitartrate)
delayed-release capsules
delayed-release oral granules

PROCYSBI MAINTAINED KIDNEY FUNCTION AT 1 AND 2 YEARS[1,11]

The effect of PROCYSBI on the kidneys was studied in adults and children aged ≥2 years[1,11]

All patients but 1 (40 out of 41 patients) who completed the phase 3 trial chose to continue on to the long-term extension trial.[1]

Kidney function* was maintained during 24 months of treatment[11]



Adapted from Langman CB, et al. *J Pediatr.* 2014.

*Kidney function was expressed as estimated glomerular filtration rate (eGFR).

Please see the full clinical trial study design for RP103-03-04 on the flashcard in the pocket of this brochure.

PROCYSBI controlled cystine levels below target throughout the study[1]

- 90% of patients (36 out of 40) continued treatment for at least 24 months
- 50% of patients (20 out of 40) continued for longer than 60 months
- Throughout the more than 60 months studied, WBC cystine levels were maintained below target (1.0 nmol ½ cystine/mg protein)

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **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.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

PROCYSBI CONTROLLED CYSTINE LEVELS IN CHILDREN AS YOUNG AS AGE 1 YEAR[1]

With PROCYSBI, mean WBC cystine concentrations were controlled below target[1]

Fourteen of the 15 patients aged 1 year to <6 years completed 12 months of treatment with PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules, and 10 patients completed 18 months of treatment.[1]

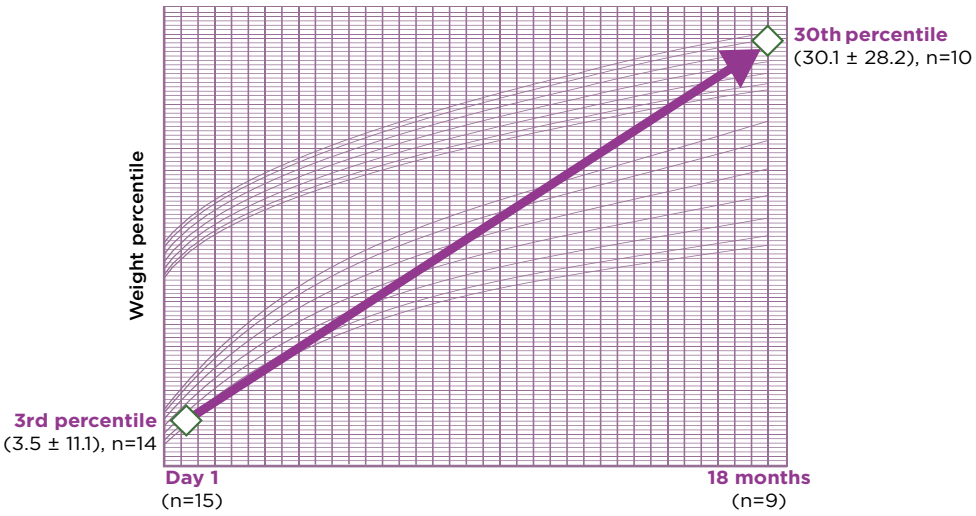
	DAY 1 (n=15)	12 MONTHS (n=13)	18 MONTHS (n=9)
Mean WBC cystine concentrations[1,†] (Target = <1.0 nmol ½ cystine/mg protein)	3.17 ± 2.95	0.80 ± 0.60	0.74 ± 0.64

[†]WBC cystine concentrations were measured 30 minutes after the morning dose.

PROCYSBI improved growth measures[1]

- Children taking PROCYSBI for 18 months (study exit) reached the 30th mean weight percentile
- In the same patients, similar trends were observed for height

PROCYSBI improved weight measures[1]



Weight z scores were -4.0 ± 2.1 at baseline, -2.2 ± 1.7 at 12 months, and -1.3 ± 2.0 at 18 months.[1]

Growth chart is for illustrative purposes only.

Please see the full clinical trial study design for RP103-08 on the flashcard in the pocket of this brochure.

SELECT IMPORTANT SAFETY INFORMATION

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 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.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

CORRECT DOSING MAY LEAD TO IMPROVED TOLERABILITY AND DISEASE CONTROL[1]

Starting dosage for capsules and packets

Starting and maintenance dosage of PROCYSBI by body weight in cysteamine-naïve patients aged ≥1 year (dosage rounded using available capsule strengths)[1]

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‡
	⅙ of dosage	¼ of dosage	
0-5	25	50	200
6-10	50	75	300
11-15	75	100	400
16-20	100	125	500
21-25	100	150	600
26-30	125	175	700
31-40	125	200	800
41-50	150	225	900
≥51	175	250	1000

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

Starting low and slowly increasing the dose may reduce the risk of some adverse events[1]

- The maintenance dosage after initial dose escalation is 1.3 g/m^2 of body surface area per day
- **Patients aged 1 year to <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
- **Patients aged ≥6 years:** Gradually increase the dosage over 4 to 6 weeks until the maintenance dosage is achieved

Switching patients from IR cysteamine bitartrate[1]

For patients switching from IR cysteamine bitartrate to PROCYSBI, the starting total daily dose of PROCYSBI is equal to their previous total daily dose of IR cysteamine bitartrate.

If tolerability issues occur with PROCYSBI[1]

If adverse events 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.

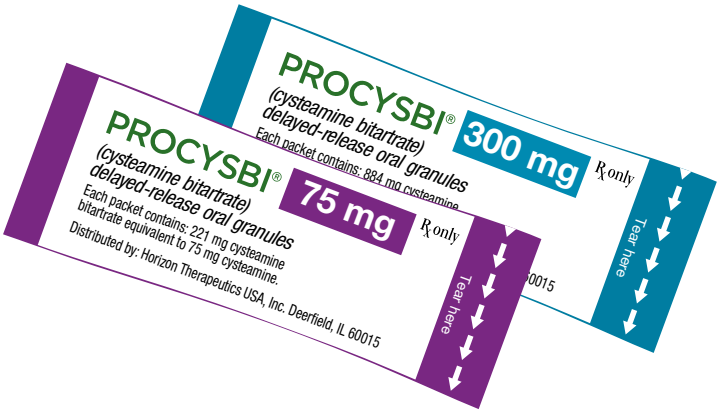
Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

PROCYSBI IS AVAILABLE IN CAPSULES AND PACKETS

PROCYSBI in capsules

PROCYSBI in packets



Both the packets and the capsules contain the same PROCYSBI microbeads that provide patients with 12 hours of continuous cystine control.[1]

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **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.

CONTRAINDICATIONS

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

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

PROCYSBI IS AVAILABLE IN CAPSULES AND PACKETS

	CAPSULES	PACKETS
Available strengths	• 25 mg • 75 mg	• 75 mg • 300 mg
How to take	At each dose, capsules can be swallowed whole, or opened and the microbeads mixed with select foods or liquids.[1]	At each dose, packets must be opened and the PROCYSBI microbeads mixed with select foods or liquids.[1]
Potential candidates	Patients who prefer to swallow whole capsules may be good candidates for PROCYSBI in capsules.	Patients who may be good candidates for PROCYSBI in packets include those who: • Take their medicine via a gastrostomy tube (G-tube) • Have trouble swallowing • Take the time to open individual capsules for each dose

Important information about dosing PROCYSBI capsules and packets[1]

- Both capsules and packets have the same recommended weight-based dosing
- When switching patients between capsules and packets, select doses may require adjustments
- Round dose calculations to the nearest incremental dose that can be administered using the available capsule or packet strengths
- Only use whole capsules or the entire contents of a packet
- When adjusting or titrating a dose, use WBC cystine level tests to confirm cystine levels are maintained below target

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

REGULAR WBC CYSTINE LEVEL TESTING IS CRITICAL TO MANAGEMENT[1]

Monitoring Frequency[1]		
Patients switching from IR cysteamine to PROCYSBI: • 2 weeks after PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules initiation • Then quarterly for 6 months • Then twice yearly (at minimum)	**Cysteamine-naïve patients aged 1 year to <6 years:** • 2 weeks after PROCYSBI initiation • Then monitor until the target WBC cystine concentration is achieved • Then monthly for 3 months • Then quarterly for 1 year • Then twice yearly (at minimum)	**Cysteamine-naïve patients aged ≥6 years:** • Obtain measurement after reaching the maintenance PROCYSBI dosage • Then monthly for 3 months • Then quarterly for 1 year • Then twice yearly (at minimum)

Monitoring Timing[1]

Obtain WBC sample 12 hours after dosing with PROCYSBI. It is important to accurately record the time of the last dose, the actual dose, and the time the blood sample was taken.

Type of Test	Testing Institution	Test-Specific Target Cystine Level[12]
Granulocytes	University of California San Diego	**Less than 1.9** nmol ½ cystine/mg protein
Mixed leukocytes	Baylor Genetics	**Less than 1.0** nmol ½ cystine/mg protein

Maintenance dose may require adjustment to achieve target WBC cystine levels[1]

If the WBC cystine concentration is greater than the target level of less than 1.0 nmol ½ cystine/mg protein, consider the following before dosage adjustment[1]:

- Adherence to medicine and dosing interval
- The timing between the last dose and the blood draw for the laboratory measurement
- The timing of PROCYSBI administration in relation to food or other administration instructions

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

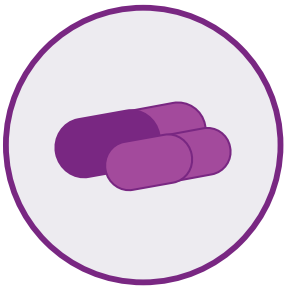
- **Central Nervous System (CNS) Symptoms:** CNS symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy have been associated with immediate-release cysteamine. Monitor for CNS symptoms; interrupt or reduce the dose for severe symptoms or those that persist or progress.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

ADMINISTRATION OPTIONS

PROCYSBI offers flexibility in administration, with 3 different ways your patients can take it.[1]

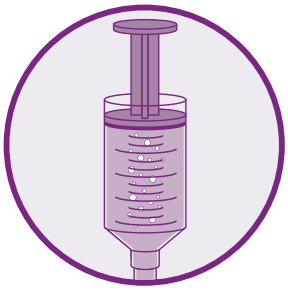


1 – SWALLOWED WHOLE

PROCYSBI capsules can be swallowed whole with fruit juice (**except grapefruit juice**) or water. Do not crush or chew the capsules.[1]

2 – OPENED AND MIXED WITH SELECT FOODS OR LIQUIDS

For patients who cannot tolerate PROCYSBI on an empty stomach or have difficulty swallowing, capsules or packets should be opened and the microbeads mixed with select foods or liquids.[1]



3 – THROUGH A G-TUBE

For individuals with a G-tube that is **size 14 French or larger**, PROCYSBI capsules or packets should be opened and the microbeads mixed with strained applesauce with no chunks.[1]

Patients should be directed to take PROCYSBI correctly for best results. They should[1]:

- Take PROCYSBI the same way each time
- Not eat for at least 2 hours before and at least 30 minutes after taking PROCYSBI
  - Take PROCYSBI with no more than ½ cup (4 oz) of food up to 1 hour before or after they take it, if they cannot tolerate PROCYSBI on an empty stomach
- Take PROCYSBI at least 1 hour before or after they take medicines that contain bicarbonate or carbonate

For approved foods and liquids and Instructions for Use, go to **PROCYSBIHCP.com**.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

PROCYSBI®
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delayed-release capsules
delayed-release oral granules

SUPPORT FOR YOUR PATIENTS

Horizon By Your Side is a patient support program dedicated to improving the lives of people with cystinosis by providing ongoing individualized support and education.

A **Patient Access Liaison (PAL)** provides dedicated, one-on-one support for your patient. They work directly with individual patients to answer non-medical, logistical questions and provide support upon enrollment. Additionally, the PAL educates about navigating insurance processes and accessing treatment on your patient's behalf. The PAL has the expertise and tools to support the patient by educating on patient benefits, prior authorization requirements, payer policies, and coding and claim submissions.

A **Case Manager** assigned to your patient may also be in touch with your office to make sure important insurance information is properly shared.

These comprehensive services are free of charge and built around 3 components: Connect, Coordinate, and Champion.

The Horizon By Your Side team will:

Connect

- Connect your patients to others living with rare diseases via live events and online resources
- Provide tools and resources to help your patients manage day-to-day challenges
- Introduce your patients to advocacy groups to provide more support and inform them of events in their area

Coordinate

- Help your patients understand their coverage and provide information about financial assistance programs
- Assist your patients in connecting with their specialty pharmacy

Champion

- Serve as a dedicated personal resource and the main point of contact for your patients' ongoing non-medical logistical needs
- Provide your patients with education and answer their non-clinical questions
- Help your patients through changes that may impact their treatment

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

PRESCRIBING PROCYSBI

A Patient Enrollment Form (PEF) is required to initiate treatment with PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules. Download the form at **PROCYSBIHCP.com**.

A completed form requires the following information:

- Patient information, including:
  - The most recent results of a WBC cystine level test
  - Recent history with CYSTAGON® (cysteamine bitartrate) capsules
  - Use of a G-tube
- Prescriber information, including all contact information for your practice or facility
- Insurance information for the patient and, if possible, copies of the patient's insurance cards for primary as well as supplementary insurance

You will also need to:

- Complete the prescription and clinical information section in its entirety
- Reference the included select PROCYSBI dosing instructions or the PROCYSBI Full Prescribing Information for complete dosing information
- Review, sign, and date the prescriber certification at the bottom of the PEF
  - In signing, you are indicating to dispense PROCYSBI as written. If a substitution is allowed, it should be noted
- Check that your patient has printed, signed, and dated the required Patient Authorization Form providing HIPAA authorization for Horizon By Your Side
  - By filling out and signing this form, the enrollment process in Horizon By Your Side has initiated; additionally, 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

The completed PEF and a copy of both sides of the patient's medical and prescription drug benefit cards should be faxed (1-877-773-9411) or emailed (HPSPRO@horizontherapeutics.com) to the Horizon By Your Side team.

Visit **PROCYSBIHCP.com** to download the PEF along with detailed instructions for completing and submitting the form.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

INDICATION AND IMPORTANT SAFETY INFORMATION

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.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

IMPORTANT SAFETY INFORMATION (continued)

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 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.

References: 1. PROCYSBI (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules [prescribing information] Horizon. **2.** Elmonem MA, Veys KR, Soliman NA, van Dyck M, van den Heuvel LP, Levtchenko E. Cystinosis: a review. *Orphanet J Rare Dis.* 2016;11(47):1-17. **3.** Gahl WA, Balog JZ, Kleta R. Nephropathic cystinosis in adults: natural history and effects of oral cysteamine therapy. *Ann Intern Med.* 2007;147(4):242-250. **4.** Nesterova G, Gahl WA. Cystinosis: the evolution of a treatable disease. *Pediatr Nephrol.* 2013;28(1):51-59. **5.** Langman CB, Barshop BA, Deschênes G, et al. Controversies and research agenda in nephropathic cystinosis: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. *Kidney Int.* 2016;89(6):1192-1203. **6.** Levtchenko EN, van Dael CM, de Graaf-Hess AC, et al. Strict cysteamine dose regimen is required to prevent nocturnal cystine accumulation in cystinosis. *Pediatr Nephrol.* 2006;21(1):110-113. **7.** Dohil R, Fidler M, Gangoiti JA, Kaskel F, Schneider JA, Barshop BA. Twice-daily cysteamine bitartrate therapy for children with cystinosis. *J Pediatr.* 2010;156(1):71-75. **8.** Dohil R, Rioux P. Pharmacokinetic studies of cysteamine bitartrate delayed-release. *Clin Pharmacol Drug Dev.* 2013;2(2):178-185. **9.** Langman CB, Greenbaum LA, Sarwal M, et al. A randomized controlled crossover trial with delayed-release cysteamine bitartrate in nephropathic cystinosis: effectiveness on white blood cell cystine levels and comparison of safety. *Clin J Am Soc Nephrol.* 2012;7(7):1112-1120. **10.** Veys KR, Besouw MT, Pinxten AM, van Dyck M, Casteels I, Levtchenko EN. Cystinosis: a new perspective. *Acta Clin Belg.* 2016;71(3):131-137. **11.** Langman CB, Greenbaum LA, Grimm P, et al. Quality of life is improved and kidney function preserved in patients with nephropathic cystinosis treated for 2 years with delayed-release cysteamine bitartrate. *J Pediatr.* 2014;165(3):528-533. **12.** Gertsman I, Johnson WS, Nishikawa C, Gangoiti JA, Holmes B, Barshop BA. Diagnosis and monitoring of cystinosis using immunomagnetically purified granulocytes. *Clin Chem.* 2016;62(5):766-772.

Please see complete IMPORTANT SAFETY INFORMATION on pages 14 and 15 and click here for the PROCYSBI Full Prescribing Information.

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

DOSING EVERY 12 HOURS FOR CONTINUOUS CYSTINE CONTROL[1]

PROCYSBI® (cysteamine bitartrate) delayed-release capsules and delayed-release oral granules is approved for use in children and adults aged ≥1 year with nephropathic cystinosis[1]

- Dosed every 12 hours (twice daily)[1]
- Proprietary delayed-release coating on PROCYSBI microbeads releases cysteamine gradually for continuous cystine control[7-10]
- Offers flexible administration options for your patients, including those with a G-tube[1]

The safety and effectiveness of PROCYSBI has been established in adults and pediatric patients aged ≥1 year for the treatment of nephropathic cystinosis[1]

In clinical trials, PROCYSBI[1]:

- Controlled cystine levels for a full 12 hours, allowing for twice-daily dosing
- Reduced cystine levels to treatment target and maintained them over time
- Maintained kidney function as measured by eGFR over 24 months
- Improved measures of height and weight in patients aged 1 year to <6 years

With PROCYSBI, you have a choice

- PROCYSBI microbeads can be prescribed in capsules and in tear-open packets. Both options contain the same medicine, but they are available in different strengths[1]

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.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

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 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.

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CLINICAL TRIAL STUDY DESIGNS FOR PROCYSBI

	RP103-03[1,9]	RP103-03-04[1,11]	RP103-08[1]
STUDY DESIGN	Multicenter, open-label, randomized, controlled, crossover clinical trial	Multicenter, single-arm, open-label, long-term extension trial	Multicenter, open-label clinical trial
PATIENTS	40 pediatric and 3 adult patients with nephropathic cystinosis, aged 6 to 26 years (mean age 12 years)	40 of 41 participants who completed the randomized trial (RP103-03) continued on to the long-term extension, plus 13 pediatric patients aged 2 to 6 years were also enrolled in the extension trial	17 patients with a documented diagnosis of nephropathic cystinosis who were naïve to cysteamine treatment (15 patients aged 1 to 5 years, 1 patient aged 9 years, and 1 patient aged 22 years)
DOSING	Patients on a stable dose of immediate-release (IR) cysteamine bitartrate were randomized to continue on their stable dose or switch to PROCYSBI at a dose of ~70% of their stable dose. PROCYSBI dose could be increased once by 20% to 25% based on peak white blood cell (WBC) cystine levels.	PROCYSBI dose was the same as at the end of the short-term study (RP103-03). Dose could be adjusted by investigator based on interval WBC cystine level. The 13 pediatric patients aged 2 to 6 years were on IR cysteamine bitartrate at trial entry.	The PROCYSBI starting dose was one-quarter of the maintenance dose of 1 g/m^2/day. The dosage was gradually increased by 10% every 2 weeks.
ENDPOINTS	Steady-state WBC cystine levels in patients treated with PROCYSBI compared to IR cysteamine bitartrate	• Number of participants with treatment-emergent adverse events • Maintenance of WBC cystine concentrations • Mean estimates of renal function, as measured by the estimated glomerular filtration rate (eGFR)	• Mean WBC cystine concentrations at 12 and 18 months • Mean weight and height percentiles at 12 and 18 months

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