



Elmiron (pentosan polysulfate sodium) Prior Authorization Program Summary

This program applies to MN Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE¹

Brand (generic)	Indication	Dosage
Elmiron® (pentosane polysulfate sodium)	The relief of bladder pain or discomfort associated with interstitial cystitis	One 100mg capsule taken three times daily

CLINICAL RATIONALE

Interstitial cystitis

Most researchers believe it is not one, but several diseases because interstitial cystitis (IC) varies so much in symptoms and severity. In recent years, bladder pain syndrome (BPS) or painful bladder syndrome (PBS) has been used to describe cases with painful urinary symptoms that may not meet the strictest definition of IC. The term IC/BPS includes all cases of urinary pain that can't be attributed to other causes, such as infection or urinary stones. The term interstitial cystitis, or IC, is used alone when describing cases that meet all of the IC criteria established by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).² The diagnosis of IC/PBS in the general population is based on: 1.) presence of pain related to the bladder, usually accompanied by frequency and urgency of urination, and 2.) absence of other diseases that could cause the symptoms.²

Clinical Guidelines

European Association of Urology (EAU)- Guidelines on Treatment of Chronic Pelvic Pain (2014)³

Interstitial cystitis (IC) describes a chronic, distressing bladder condition. A so-called ulcer is a typical cystoscopic finding in 10-50% of IC patients. IC encompasses a heterogeneous spectrum of disorders, with different endoscopic and histopathological presentations, with inflammation an important feature in only a subset of patients. To embrace all patients suffering from bladder pain, the terms painful bladder syndrome (PBS) or BPS have been suggested as more accurate when referring to pain in the bladder region, while assuming IC with Hunner's lesion as a specific type of chronic inflammation of the bladder. The term BPS was put forward by the International Society for the Study of BPS (ESSIC) and is used in these guidelines; Classic IC (Hunner's lesion and inflammation) is referred to as BPS type 3 C.

The recommendations in this guideline are given a grade of A, B or C based on the following: Grade A= Based on clinical studies of good quality and consistency (≥ 1 RCT); Grade B= Well conducted clinical studies, without RCTs; Grade C=Recommended despite absence of directly applicable studies of good clinical quality.

Treatments given a Grade A recommendation include:

- Multimodal behavioural, physical and psychological techniques should always be considered alongside oral or invasive treatments of BPS
- Hydroxyzine
- Amitriptyline
- Pentosanpolysulphate sodium
- Treatment with oral pentosanpolysulphate sodium plus subcutaneous heparin is recommended especially in low responders to pentosanpolysulphate sodium alone
- Administer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods
- Administer intravesical pentosanpolysulphate sodium before more invasive treatment alone or combined with oral pentosanpolysulphate sodium alone
- Administer intravesical dimethyl sulphoxide (DMSO) before more invasive measures
- Administer submucosal injection of BTX-A plus hydrodistension if intravesical instillation therapies have failed
- All ablative organ surgery should be the last resort for experienced and BPS knowledgeable surgeons only

Treatments given a Grade B recommendation include:

- Cimetidine before invasive treatments
- Cyclosporin A might be used in BPS but adverse effects are significant and should be carefully considered
- Intravesical hyaluronic acid before more invasive measures
- Intravesical chondroitin sulphate before more invasive measures
- Transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only
- Neuromodulation might be considered before more invasive interventions
- Bladder training in patients with little pain
- Manual and physical therapy in first approach.

American Urologic Association [AUA] - Guidelines on Treatment of Interstitial Cystitis/Bladder Pain Syndrome [IC/BPS] (June, 2011, amended 2014)⁴

AUA categorizes body of evidence strength as: Grade A (well-conducted RCTs or exceptionally strong observational studies), Grade B (RCTs with some weaknesses of procedure, generalizability, or generally strong observational studies), or Grade C (observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data).

First-, second-, third-, fourth-, fifth-, and sixth-line treatment hierarchy was derived by balancing the potential benefits to the patient with the invasiveness of the treatment, the duration and severity of potential adverse events, and the reversibility of potential adverse events. It is important that this hierarchy was not established based on evidence strength.

- First line treatments should be performed on all patients (Evidence Grade A).
 - Patients should be educated about normal bladder function, what is known and not known about IC/BPS, benefits vs risks/burdens of the available treatment alternatives, the fact that no single treatment has been found effective for the majority of patients and the fact that acceptable symptom control may require trials of multiple therapeutic options (including combination therapy) before it is achieved.
 - Self-care practices and behavioral modifications that can improve symptoms should be discussed and implemented as feasible.
 - A trial of over-the-counter products (phenazopyridine [Pyridium], nutraceuticals [Quercetin], or calcium glycerophosphate [Preliief]) is commonly initiated by patients themselves and, although data in the literature

are limited, individual patients may find some to be worthwhile in alleviating symptoms.

- Second line treatments: Appropriate manual physical therapy techniques, if appropriately trained clinicians are available, should be offered. Pelvic floor strengthening exercises (e.g. Kegel exercises) should be avoided.
 - Multimodal pain management approaches (e.g., pharmacological, stress management, manual therapy if available) should be initiated.
 - These medications are grouped together as second line treatments because their administration is associated with minor adverse events and efficacy for any individual is unpredictable (listed in alphabetical order; no hierarchy implied).
 - Amitriptyline, cimetidine, hydroxyzine or pentosan polysulfate may be administered as second line oral medications. All got an evidence grade of B, except hydroxyzine, which got a C.
 - Dimethyl sulfoxide, heparin or lidocaine may be administered as second line intravesical treatments. Lidocaine got an evidence grade of B, the others got C.
- Third line treatments: Cystoscopy under anesthesia with short-duration (<10 minutes), low pressure (60 to 80 cm of water) hydrodistension. Hunner's lesions can be taken off with electrodes, laser, or injected with the steroid triamcinolone (Kenalog). Evidence grade of C.
- Fourth line treatments: Neurostimulation may be done for frequency/urgency relief but has not shown evidence of effectiveness. Evidence grade of C.
- Fifth line treatments: Cyclosporine when justified as the risk of side effects is high. Botulinum toxin A (Botox) injections into bladder muscle when justified as side effects can be difficult such as painful urination and required catheterization. Evidence grade of C.
- Sixth line treatment: Major surgery of bladder removal, enlargement, or urinary diversion) when all else has failed. Evidence grade of C.

Efficacy¹

Pentosan polysulfate sodium is a low molecular weight heparin-like compound. It has anticoagulant and fibrinolytic effects. The mechanism of action of pentosane polysulfate sodium in interstitial cystitis is unknown.

Elmiron Dosing: Elmiron is administered as an oral 100 mg capsule. The usual schedule is 300 mg/day taken as one 100 mg capsule orally three times daily. The capsules should be taken with water at least 1 hour before meals or 2 hours after meals. Patients should be reassessed after 3 months of treatment and may continue treatment for an additional 3 months if no improvement occurs. It is important to note that clinical value or risks of continued treatment in patients whose pain has not improved by 6 months is not known.

Elmiron Safety

Contraindications: Elmiron (pentosan polysulfate sodium) is contraindicated in patients with known hypersensitivity to the drug, structurally related compounds, or excipients.

REFERENCES

1. Elmiron Prescribing Information. Janssen Pharmaceuticals, Inc. December 2012.
2. Hanno, Philip, MD. "Interstitial Cystitis/Painful Bladder Syndrome." *Interstitial Cystitis/Painful Bladder Syndrome*. National Kidney and Urologic Diseases Information Clearinghouse, 29 June 2012. Web. 05 July 2013.
3. European Association of Urology (EAU, 2014). Guidelines on treatment of chronic pelvic pain. Available at: http://www.uroweb.org/gls/pdf/26%20Chronic%20Pelvic%20Pain_LR.pdf.

4. Hanno, Philip M., David A. Burks, and J. Q. Clemens. "DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME." *American Urological Association (AUA) Guideline*. American Urological Association, Jan. 2011. Available at: <http://www.auanet.org/common/pdf/education/clinical-guidance/IC-Bladder-Pain-Syndrome.pdf>.

Elmiron (pentosan polysulfate sodium) Prior Authorization

TARGET AGENT

Elmiron® (pentosan polysulfate sodium)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial Evaluation

Target Agent will be approved for initial use when ALL of the following are met:

1. The patient has a diagnosis of interstitial cystitis (IC) or interstitial cystitis/bladder pain syndrome (IC/BPS) or interstitial cystitis/painful bladder syndrome (IC/PBS)
AND
2. The patient has tried and had an inadequate response to behavioral modification or self-care practices
AND
3. ONE of the following:
 - a. The patient has tried and had an inadequate response to phenazopyridine, hydroxyzine, cimetidine or amitriptyline
OR
 - b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to phenazopyridine, hydroxyzine, cimetidine or amitriptyline**AND**
4. The patient does not have any FDA labeled contraindications to the requested agent
AND
5. The dose requested does not exceed the FDA labeled dose

Length of Approval: 6 months

Renewal Evaluation

Target Agent will be approved for renewal when ALL of the following are met:

1. The patient has been approved for the requested agent through the Prime Therapeutics Prior Authorization process
AND
2. The patient has received benefit from the requested agent (e.g. decreased bladder pain, decreased frequency or urgency of urination)
AND
3. The patient does not have any FDA labeled contraindications to the requested agent
AND
4. The dose requested does not exceed the FDA labeled dose

Length of Approval: 12 months



Step Therapy Supplement Program Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
 - a. A statement by the prescriber that the patient is currently taking the requested agent
AND
 - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
AND
 - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
- OR**
2. BOTH of the following
 - a. The patient's medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
 - i. Evidence of a paid claim(s) within the past 999 days
OR
 - ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days**AND**
 - b. ONE of the following:
 - i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
OR
 - ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)
- OR**
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria