

## Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome

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### Abbreviations and Acronyms

AE = Adverse events

AUA = American Urological Association

BCG = Bacillus Calmette-Guerin

BTX-A = Onabotulinumtoxin A

CISC = Clean intermittent self-catheterization

CyA = Cyclosporine A

DMSO = Dimethylsulfoxide

GUPI = Genitourinary pain index

IC/BPS = Interstitial cystitis/bladder pain syndrome

ICSI = Interstitial cystitis symptom index

NSAIDs = Non-steroidal anti-inflammatory drugs

PPS = Pentosan polysulfate

QoL = Quality of life

RCT = Randomized controlled trials

VAS = Visual analog scale

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**Purpose:** This guideline provides direction to clinicians and patients regarding how to recognize interstitial cystitis/bladder pain syndrome (IC/BPS), conduct a valid diagnostic process, and approach treatment with the goals of maximizing symptom control and patient quality of life while minimizing adverse events and patient burden.

**Methods:** An initial systematic review of the literature using the MEDLINE® database (search dates 1/1/83-7/22/09) was conducted to identify peer-reviewed publications relevant to the diagnosis and treatment of IC/BPS. The review yielded an evidence base of 86 treatment articles after application of inclusion/exclusion criteria. In July 2013, the Guideline underwent an Update Literature Review, a process in which an additional literature search is conducted and a systematic review is produced in order to maintain guideline currency with newly published literature. The 2013 review identified an additional 31 articles relevant to treatment. An Update Literature Review in 2022 (search dates: 06/2013—01/2021) identified 63 studies, 53 of which were added to the evidence base.

**Results:** In contrast to the prior versions, the 2022 updated Guideline no longer divides treatments into first-line through sixth-line tiers. Instead, treatment is categorized into behavioral/non-pharmacologic, oral medicines, bladder instillations, procedures, and major surgery. This approach reinforces that the clinical approach for IC/BPS needs to be individualized and based on the unique characteristics of each patient. In addition, new statements were written to provide guidance on cystoscopy for patients with Hunner lesions, shared decision-making, and potential adverse events from pentosan polysulfate. The supporting text on major surgery also has been completely revised.

**Conclusion:** IC/BPS is a heterogeneous clinical syndrome. Even though patients present with similar symptoms of bladder/pelvic pain and pressure/discomfort associated with urinary frequency and strong urge to urinate, there are subgroups or phenotypes within IC/BPS. Except for patients with Hunner lesions, initial treatment should typically be nonsurgical. Concurrent, multi-modal therapies may be offered.

**Key Words:** pelvic pain, treatment, quality of life, guideline, review

### GUIDELINE STATEMENTS

#### Diagnosis of IC/BPS

**Guideline Statement 1.** The basic assessment should include a careful

history, physical examination, and laboratory examination to document symptoms and signs that characterize IC/BPS and exclude other disorders that could be the

**cause of the patient's symptoms. Clinical Principle**

The clinical diagnosis of IC/BPS requires a careful history, physical examination, and laboratory examination to document basic symptoms that characterize the disorder and exclude infections or other confusable disorders. IC/BPS is a chronic disorder and symptoms should be present for at least six weeks with documented negative urine cultures. The number of voids per day, sensation of constant urge to void, and the location, character, and severity of pain, pressure, or discomfort should be documented. Dyspareunia, dysuria, ejaculatory pain in men, and the relationship of pain to menstruation in women should also be noted. A brief neurological exam to rule out an occult neurologic problem and an evaluation for incomplete bladder emptying to rule out occult retention should be done on all patients. A proper hematuria workup should be performed in patients with un-evaluated hematuria, and considered in patients with tobacco exposure given the high risk of bladder cancer in smokers.<sup>1</sup> Urine culture may be indicated even in patients with a negative urinalysis in order to detect lower levels of bacteria that are clinically significant but not readily identifiable with a dipstick or on microscopic exam.

**Guideline Statement 2. Baseline voiding symptoms and pain levels should be obtained in order to measure subsequent treatment effects. Clinical Principle**

It is important to establish baseline values in order to evaluate later treatment responses. A one-day voiding log, at the very least, should be used to establish the presence of a low volume frequency voiding pattern that is characteristic of IC/BPS. Very low voiding frequencies or high voided volumes should prompt a diligent search for an alternate diagnosis. Pain should be evaluated using the genitourinary pain index (GUPI), interstitial cystitis symptom index (ICSI), or visual analog scale (VAS) in order to gather information regarding pain/discomfort location(s), intensity, characteristics, and to identify factors that exacerbate or alleviate pain or discomfort (eg, the presence of painful bladder filling or painful urgency). This information establishes a diagnosis of IC/BPS and provides a baseline against which treatments can be evaluated.

**Guideline Statement 3. Cystoscopy and/or urodynamics should be considered when the diagnosis is in doubt; these tests are not necessary for making the diagnosis in uncomplicated presentations. Expert Opinion**

Cystoscopy and urodynamic testing are appropriate when the IC/BPS diagnosis is in doubt or cystoscopy can guide therapy and exclude conditions that may

mimic IC/BPS such as bladder cancer, bladder stones, and intravesical foreign bodies. Suspicion of these entities is an indication for the diagnostic use of cystoscopy.

There are no agreed-upon cystoscopic findings diagnostic for IC/BPS; the only consistent cystoscopic finding that leads to a diagnosis is the appearance of Hunner lesions. Likewise, there are no agreed-upon urodynamic criteria diagnostic for IC/BPS. Specific indications that urodynamic evaluation may be useful include suspicion of outlet obstruction in either sex, possibility of poor detrusor contractility, or other conditions that could explain why patients are refractory to behavioral or medical therapies. In general, however, urodynamics are not recommended for routine clinical use to establish an IC/BPS diagnosis.

**Guideline Statement 4. Cystoscopy should be performed in patients for whom Hunner lesions are suspected. Expert Opinion**

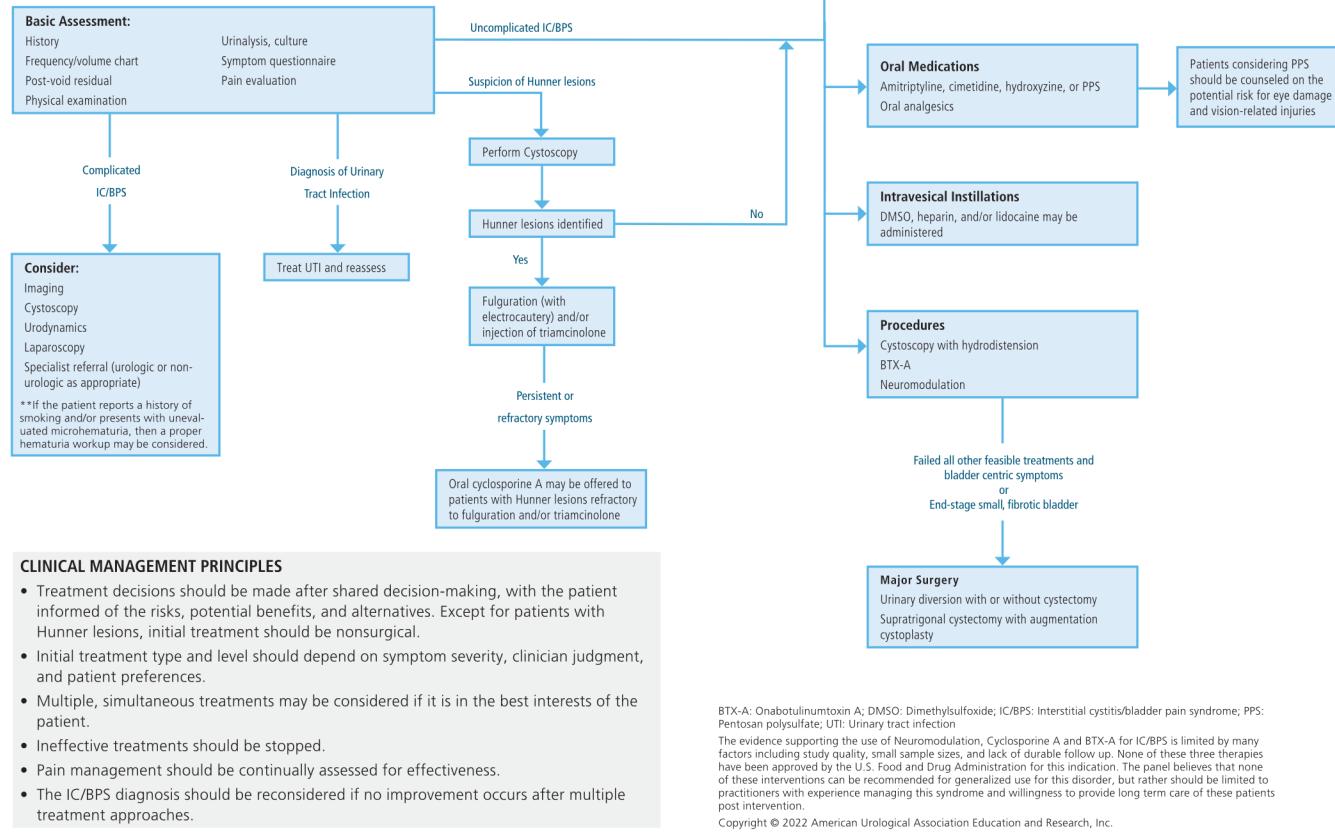
Cystoscopy remains the only reliable way to diagnose the presence of Hunner lesions. Although most IC/BPS patients may tolerate office flexible cystoscopy without hydrodistention of the bladder, some may prefer to have cystoscopy performed under general anesthesia. Most patients with Hunner lesions will respond to treatment, therefore, early diagnosis by cystoscopy is recommended in patients suspected to have these lesions, without requiring them to fail other behavioral or medical treatments. If Hunner lesions are found on cystoscopy, triamcinolone injection and/or fulguration can be performed; for those who fail triamcinolone and/or fulguration, oral Cyclosporine A (CyA) and/or other multi-modal therapies may be offered (see Figure).

Since the odds of identifying Hunner lesions are higher in patients over the age of 50,<sup>2</sup> it is reasonable to offer cystoscopy to men and women over the age of 50. Cystoscopy should also be considered in those who fail conventional therapies but have never had a cystoscopy before to evaluate for the presence or absence of Hunner lesions. In patients who report abnormal findings in previous cystoscopy, and it is unclear to the clinician what the abnormal findings are, cystoscopy may be performed to visualize directly. In the Panel's opinion, performing cystoscopy for every IC/BPS patient is not advisable since the benefits/risks ratio is unfavorable for younger patients who have a much lower prevalence of Hunner lesions.

**Management Approach to IC/BPS**

**Guideline Statement 5. Treatment decisions should be made after shared decision-making, with the patient informed of the risks, potential benefits, and alternatives. Except for patients with Hunner lesions, initial treatment**

IC/BPS: An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.



**Figure.** IC/BPS Diagnosis and Treatment Algorithm.

### should typically be nonsurgical. *Expert Opinion*

**Guideline Statement 6. Efficacy of treatment should be periodically reassessed, and ineffective treatments should be stopped. Clinical Principle**

**Guideline Statement 7. Multimodal pain management approaches (eg, pharmacological, stress management, manual therapy if available) should be initiated. Pain management should be continually assessed for effectiveness because of its importance to quality of life. If pain management is inadequate, then consideration should be given to a multidisciplinary approach and the patient referred appropriately. Clinical Principle**

**Guideline Statement 8. The IC/BPS diagnosis should be reconsidered if no improvement occurs after multiple treatment approaches. Clinical Principle**

Because the underlying pathophysiology of IC/BPS is unknown, treatment goals are to manage symptoms

and optimize quality of life (QoL). Effective pain management is an important component of QoL and, particularly for complex patient presentations, may require a multidisciplinary, multimodal approach. IC/BPS treatment alternatives are characterized by the fact that most treatments may benefit a subset of patients but that no treatment reliably benefits most or all patients. While some patients may opt to start with education, behavior modification, or physical therapy alone to treat IC/BPS, other patients will benefit from concomitant oral and/or intravesical treatments. As part of shared decision-making, clinicians should counsel patients on all applicable options, with their risks and benefits. It is not uncommon for a particular patient to experience lack of benefit from a particular treatment; therefore, if a clinically meaningful trial of a therapy has been conducted without efficacy, then the therapy should be discontinued, and other therapeutic alternatives should then be considered. If the usual IC/BPS therapies provide no improvement in symptoms, then the clinician should revisit the diagnosis of IC/BPS and consider whether an unidentified disorder may be

present that is producing symptoms. This consideration may require additional diagnostic workup and/or referral to appropriate specialists.

### Treatment Categories of IC/BPS

**Behavioral/Non-pharmacologic Treatments.** *Guideline Statement 9*

**Patients should be educated about normal bladder function, what is known and not known about IC/BPS, the benefits versus 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. *Clinical Principle***

Patients should be made aware that IC/BPS is typically a chronic disorder requiring continual and dynamic management. Adequate symptom control is achievable but may require trials of multiple therapeutic options to identify the regimen that is effective for that patient. Patients should be informed that, given the chronic nature of IC/BPS, the typical course involves symptom exacerbations and remissions.

*Guideline Statement 10*

**Self-care practices and behavioral modifications that can improve symptoms should be discussed and implemented as feasible. *Clinical Principle***

Clinical experience and a limited literature suggest that modifying certain behaviors can improve symptoms in some IC/BPS patients.<sup>3</sup> Patients should become aware of and avoid specific behaviors that worsen symptoms. Behavioral modification strategies may include: altering the concentration and/or volume of urine, either by fluid restriction or additional hydration; avoidance of certain foods known to be common bladder irritants; use of an elimination diet to determine which foods or fluids may contribute to symptoms; over-the-counter products (eg, nutraceuticals, calcium glycerophosphates, phenazopyridine); techniques applied to trigger points and areas of hypersensitivity (eg, application of heat or cold over the bladder or perineum); strategies to manage IC/BPS flare-ups (eg, meditation, imagery); pelvic floor muscle relaxation; and bladder training with urge suppression. Other controllable behaviors or conditions that may worsen symptoms in some patients include certain types of exercise (eg, pelvic floor muscle exercises), sexual intercourse, wearing of tight-fitting clothing, and the presence of constipation.

*Guideline Statement 11*

**Patients should be encouraged to implement stress management practices to improve coping techniques and manage stress-induced symptom exacerbations. *Clinical Principle***

Psychological stress is associated with heightened pain sensitivity in general and in IC/BPS patients specifically. Effective coping with family, work, and/or past traumatic experiences is an important component of symptom management. Recommendations for specific coping strategies are beyond the scope of this guideline; however, clinicians and patients should be cognizant of stressors as triggers for symptom exacerbation and patients should be encouraged and assisted to seek appropriate support for these issues from stress management or psychological counselors.

*Guideline Statement 12*

**Appropriate manual physical therapy techniques (eg, maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions), if appropriately trained clinicians are available, should be offered to patients who present with pelvic floor tenderness. Pelvic floor strengthening exercises (eg, Kegel exercises) should be avoided. *Standard (Evidence Strength: Grade A)***

Many patients with IC/BPS exhibit tenderness and/or banding of the pelvic floor musculature, along with other soft tissue abnormalities.<sup>4</sup> It is not known whether those muscular abnormalities are primary pain generators (giving rise to associated secondary bladder pain) or are themselves secondary phenomena elicited by the primary bladder pain of IC/BPS. When such soft tissue abnormalities are present, manual physical therapy can provide symptom relief.<sup>5</sup>

Appropriate manual physical therapy techniques include maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points; lengthen muscle contractures; and release painful scars and other connective tissue restrictions.<sup>6</sup> In the absence of appropriate expertise, routine forms of pelvic physical therapy that are primarily aimed at strengthening of the pelvic floor are not recommended.

*Guideline Statement 13*

**Clinicians may prescribe pharmacologic pain management agents (eg, urinary analgesics, acetaminophen, NSAIDs, opioid/non-opioid medications) after counseling patients on the risks and benefits. Pharmacological pain management principles for IC/BPS should be similar to those for management of other chronic pain conditions. *Clinical Principle***

Despite the fact that IC/BPS is a chronic pain syndrome, little is known about effective pharmacological treatment for chronic pain in these patients. These treatments include urinary analgesics, NSAIDs, narcotics, and a wide variety of nonnarcotic medications

used for other chronic pain conditions. Please note that none of these treatments are indicated specifically for IC/BPS. Pain management alone typically does not constitute sufficient treatment for IC/BPS; a multimodal approach in which pharmacologic agents are combined with other therapies is likely to be the most effective. To the extent possible, it is essential that patients also are treated for the underlying bladder related symptoms. Due to the global opioid crisis, the judicious use of chronic opioids is advised and only after informed shared decision-making with patients and with periodic follow-ups to assess efficacy, adverse events (AEs), compliance, and potential of abuse or misuse. Non-opioids alternatives to manage pain should be used preferentially.<sup>7</sup>

### **Oral Medications**

**Guideline Statement 14.** Amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate may be administered as oral medications (listed in alphabetical order; no hierarchy is implied). **Option (Evidence Strength: Grades B, B, C, and B)**

*Amitriptyline (Evidence Strength: Grade B)*

Amitriptyline has been shown to be superior to placebo to improve symptoms of IC/BPS; however, AEs are common and, although not life-threatening, have substantial potential to compromise QoL (eg, sedation, drowsiness, nausea).<sup>8</sup> Available data suggest that beginning at low doses (eg, 10 mg) and titrating gradually to 75-100 mg if tolerated is an acceptable dosing regimen.

*Cimetidine (Evidence Strength: Grade B)*

Cimetidine has been reported to have clinically significant improvement of IC/BPS symptoms, pain, and nocturia with no AEs reported.<sup>9</sup>

*Hydroxyzine (Evidence Strength: Grade C)*

Oral hydroxyzine has been shown to result in clinically significant improvement compared to placebo.<sup>10</sup> Some studies indicate that patients who report clinically significant improvement have systemic allergies; this patient population may be more likely to respond to hydroxyzine.<sup>11</sup> AEs were common and generally not serious (eg, short-term sedation, weakness).

*Pentosan polysulfate (Evidence Strength: Grade B)*

Pentosan polysulfate (PPS) is the only FDA-approved oral agent for the treatment of IC/BPS and is by far the most-studied oral medication in use for IC/BPS. Results on the effectiveness of PPS have been contradictory; some trials report no differences in symptom improvement,<sup>10,12</sup> while others show that PPS patients improved compared to those on placebo.<sup>13–15</sup> Overall, it is the opinion of the Panel that the benefits and risks of PPS should be discussed with the patient before initiating or continuing treatment.

**Guideline Statement 15.** Clinicians should counsel patients who are considering pentosan polysulfate on the potential risk for macular damage and vision-related injuries. **Clinical Principle**

There have been recent reports of a unique retinal pigmentary maculopathy that is associated with PPS use. Symptoms have included difficulty reading, slow adjustment to low or reduced light environments, and blurred vision. The initial evidence consisted of case reports and small case series, but subsequent large retrospective cohort studies have confirmed the association.<sup>16–18</sup> The prevalence of maculopathy varies widely in PPS users but appears to be related to the cumulative amount of PPS exposure. Given these concerns, the FDA approved a new warning label for PPS in June 2020<sup>19</sup> which states that:

- A detailed ophthalmologic history should be obtained in all patients prior to starting treatment with PPS.
- For patients with preexisting ophthalmologic conditions, a comprehensive baseline retinal examination is recommended prior to starting therapy.
- In addition, a retinal examination is suggested for all patients within six months of initiating treatment and periodically while continuing treatment. If pigmentary changes in the retina develop, then risks and benefits of continuing treatment should be reevaluated, since these changes may be irreversible.

**Guideline Statement 16.** Oral cyclosporine A may be offered to patients with Hunner lesions refractory to fulguration and/or triamcinolone. **Option (Evidence Strength: Grade C)**

The data on oral CyA suggest clinically significant improvement of IC/BPS symptoms compared to patients on PPS,<sup>20</sup> particularly in patients with Hunner lesions or with active bladder inflammation.<sup>21</sup> However, because of the relatively small number of patients treated, the lack of long-term follow-up data on large numbers of patients, and the potential for serious AEs (eg, immunosuppression, nephrotoxicity), the Panel recommends that patients taking CyA should be closely monitored, especially for renal function and blood pressure.

### **Intravesical Instillations**

**Guideline Statement 17.** DMSO, heparin, and/or lidocaine may be administered as intravesical treatments (listed in alphabetical order; no hierarchy is implied). **Option (Evidence Strength: Grades C, C, and B)**

*DMSO (Evidence Strength: Grade C)*

DMSO instillation has been shown to be efficacious in improving urodynamic and voiding parameters as compared to placebo,<sup>22</sup> to bacillus Calmette-

Guerin (BCG),<sup>23</sup> and in observational studies.<sup>24–26</sup> DMSO is rapidly absorbed into the bladder wall and longer periods of holding are associated with significant pain, therefore if DMSO is used, then the panel suggests limiting instillation dwell time to 15–20 minutes. DMSO is often administered as a part of a “cocktail” that may include heparin, hydrocortisone, sodium bicarbonate, a local steroid, a lidocaine preparation, bupivacaine, and/or triamcinolone.<sup>27,28</sup> If a clinician chooses to administer a “cocktail” preparation, then he or she should be aware that DMSO potentially enhances absorption of other substances, creating the possibility for toxicity from drugs such as lidocaine.

*Heparin (Evidence Strength: Grade C)*

Observational studies of intravesical heparin<sup>29</sup> and clinical trials of patients randomized heparin in combination with alkalinized lidocaine<sup>30</sup> report clinically significant improvement in symptom relief compared to patients who were given placebo.

*Lidocaine (Evidence Strength: Grade B)*

Lidocaine has been shown to significantly improve symptoms in the short-term (ie, less than two weeks) compared to placebo. Alkalization increases urothelial penetration of lidocaine and therefore is expected to improve efficacy, but it also can increase systemic absorption and potential toxicity. No published studies have directly compared lidocaine with and without alkalinization. Patients who are given lidocaine in combination with heparin<sup>31</sup> or PPS<sup>32</sup> have been shown to exhibit relief of symptoms and a significant reduction of bladder pain and urgency compared to lidocaine alone.

## Procedures

**Guideline Statement 18. Cystoscopy under anesthesia with short-duration, low-pressure hydrodistension may be undertaken as a treatment option. Option (Evidence Strength: Grade C)**

Cystoscopy under anesthesia with low-pressure short duration hydrodistension allows the clinician to inspect the bladder for other potential causes (eg, stones, tumors) of IC/BPS and/or Hunner lesions. Mild distension makes Hunner lesions easier to identify when cracking and mucosal bleeding become evident. Distension also allows for disease “staging” by determining anatomic, as opposed to functional, bladder capacity and identifying the subset of patients who suffer reduced capacity as a result of fibrosis.

If no bladder abnormalities or ulcers are found, then the distension may proceed and serve as a treatment. Studies report that one or two exposures to low-pressure, short-duration hydrodistension can result in clinically significant relief of bladder pain

and does not decrease bladder capacity, even with multiple procedures.<sup>33</sup> However, benefits must be balanced against the possibility of a (usually temporary) flare of symptoms after distention. If Hunner lesions are detected, then their treatment is recommended.

**Guideline Statement 19. If Hunner lesions are present, then fulguration (with electrocautery) and/or injection of triamcinolone should be performed. Recommendation (Evidence Strength: Grade C)**

If Hunner lesions are found, fulguration with electrocautery,<sup>34</sup> triamcinolone injection,<sup>35,36</sup> or triamcinolone injection after electrocautery can be used to improve clinical symptoms (eg, urinary frequency, urgency, pain) and QoL. Hunner lesion treatment appears to constitute one of the few IC/BPS therapies that results in improvement measured in months with only a single exposure to the procedure. Multiple electrocauterizations of Hunner lesions did not diminish bladder capacity significantly but the number of electrotherapies was negatively correlated with the change in bladder capacity.<sup>34</sup> However, symptoms can recur and patients should be counseled that periodic retreatment is likely to be necessary as patients response decreases over time.

**Guideline Statement 20. Intradetrusor onabotulinumtoxin A may be administered if other treatments have not provided adequate improvement in symptoms and quality of life. Patients must be willing to accept the possibility that intermittent self-catheterization may be necessary. Option (Evidence Strength: Grade C)**

Intradetrusor onabotulinumtoxin A (BTX-A) can be used to treat IC/BPS symptoms either alone<sup>37</sup> or in combination with hydrodistension.<sup>38</sup> Patients typically experience symptom relief for several months with a return to baseline symptom levels over time. Common AEs included dysuria, the need for abdominal straining to void, large post-void residuals (greater than 100 mL), and the need for clean intermittent self-catheterization (CISC).

There are some interpretive challenges of the BTX-A literature given that injection sites vary across studies (trigonal, lateral, or posterior walls) and that some studies appear to use overlapping patient groups and do not constitute independent replications. Furthermore, there is a dearth of placebo-controlled trials of BTX-A alone and, in the absence of these studies, the true effect of BTX-A is not possible to determine.

Patients must be willing to accept the possibility that CISC may be necessary post-treatment. This option is not appropriate for patients who cannot

tolerate catheterization and is relatively contraindicated for patients with evidence of impaired bladder emptying. Given the potential short-term efficacy of BTX-A in the context of a possibly serious AE profile, the Panel recommends that the decision to use intradetrusor BTX-A is made in the context of shared decision-making.

**Guideline Statement 21.** A trial of neuro-modulation may be performed if other treatments have not provided adequate symptom control and quality of life improvement. If a trial of nerve stimulation is successful, then the permanent neurostimulation device may be implanted. **Option (Evidence Strength: Grade C)**

It is important to note that neuromodulation is not currently FDA-approved for IC/BPS treatment; however, many patients meet the frequency/urgency indication for which sacral neuro-modulation is approved. Given the invasiveness of the procedure and the lack of long-term follow-up data on a sufficient number of patients, the Panel judged that sacral/pudendal neurostimulation may be effective in carefully selected patients and this decision should be left to the individual clinician and patient. Clinicians and patients are cautioned that the procedure is indicated for frequency/urgency symptoms and is much less effective and potentially ineffective for pain.<sup>39,40</sup>

### Major Surgery

**Guideline Statement 22.** Major surgery (substitution cystoplasty, urinary diversion with or without cystectomy) may be undertaken in carefully selected patients with bladder-centric symptoms, or in the rare instance when there is an end-stage small fibrotic bladder, for whom all other therapies have failed to provide adequate symptom control and quality of life improvement. **Option (Evidence Strength: Grade C)**

Major surgery is irreversible, life-altering, and should be reserved for patients who have exhausted all other feasible options and whose symptoms are caused by the bladder. Patient selection has by far the greatest influence on outcome and clinicians must be rigorous in patient selection. While some patients have complete or near-complete symptom resolution after surgery, others have poor outcomes including persistent pain that can lead to suicide<sup>41</sup> (even if the bladder is removed), complications, or new symptoms with lifelong significant bother. The best-documented predictors of success are presence of Hunner lesions and small bladder capacity under anesthesia. Published evidence is limited by small numbers of patients and heterogeneity in patient selection, surgical methods, and outcome reporting.

For these reasons, uncertainty exists in the overall balance between benefits and risks/burdens. The Panel notes that major surgery should be performed only by surgeons with extensive experience in IC/BPS and dedication to long-term care for the patient.

### Treatments That Should Not Be Offered

**Guideline Statement 23.** Long-term oral antibiotic administration should not be offered. **Standard (Evidence Strength: Grade B)**

Given the non-significant findings from published studies and the potential hazards associated with long-term antibiotic administration in general (eg, fostering of antibiotic resistant organisms), the Panel judged that antibiotic treatment is contraindicated in patients who have previously been administered antibiotics without efficacy and who present with a negative urine culture.

**Guideline Statement 24.** Intravesical instillation of bacillus Calmette-Guerin should not be offered outside of investigational study settings. **Standard (Evidence Strength: Grade B)**

Long-term follow-up data on the efficacy of intravesical instillation of BCG indicate that it is not significantly greater than placebo<sup>42</sup> and BCG exposure can lead to potentially serious AEs, (eg, sepsis and other serious AEs, including death).<sup>43</sup> The risks/burdens of BCG outweigh its benefits for IC/BPS patients in routine clinical care situations; therefore, BCG administration in this patient group should be restricted to investigational settings.

**Guideline Statement 25.** High-pressure, long-duration hydrodistension should not be offered. **Recommendation (Evidence Strength: Grade C)**

High-pressure, long-duration hydrodistension is associated with increased frequency of bladder rupture, sepsis, and an inconsistent increase in benefit.<sup>44</sup> The Panel recommends that this treatment not be offered given the lack of predictable efficacy in the context of serious AEs.

**Guideline Statement 26.** Systemic (oral) long-term glucocorticoid administration should not be offered. **Recommendation (Evidence Strength: Grade C)**

Systemic long-term glucocorticoid administration should not be offered as the primary treatment for IC/BPS symptoms. Although high rates of efficacy have been reported, the Panel recommends that this therapy not be used long-term given the relatively serious AEs (eg, new diabetes onset, exacerbation of existing diabetes, pneumonia with septic shock, increased blood pressure).<sup>45,46</sup> This does not preclude the use of short-term glucocorticoid therapy to manage symptom flares.

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