

## Cystistat® – Get on with Life

a report by

**Bioniche Life Sciences Inc.**

### Management of Interstitial Cystitis

Often characterised by severe symptoms such as chronic pain, urgency and frequency, interstitial cystitis (IC) is a chronic idiopathic inflammatory bladder disease, which is frequently misdiagnosed. The disease has a significant negative impact on a patient's general lifestyle, with the frequent need to urinate and chronic pain being experienced. Incidence data suggest a large cohort of IC patients in developed countries (60/100,000 in the US, 450/100,000 in Finland). While IC is commonly regarded as a chronic debilitating disease characterised by intractable pain and urge, this is only true for the end stage of a disease that starts years or decades before, with either minor or moderate bladder symptoms. Treated at an early stage, IC may be cured in a high percentage of cases and patients spared the fate of a shrunken or painful bladder.

IC has been recognised for more than a century with, to date, an undefined aetiology. The theory of disruption of the epithelial permeability barrier is one of the most popular hypotheses thus far. The surface of the urothelium is covered with a glycosaminoglycan (GAG) layer which forms a physical barrier shielding the bladder surface from pathogens, microcrystals, proteins and even carcinogenic substances. In an IC patient, this GAG layer, which protects the bladder wall from the toxic effects of urine, is believed to be deficient, allowing substances in the urine to penetrate the bladder wall and trigger IC symptoms.

Many therapies have been used to treat IC symptoms, although there is no single effective therapy for a large percentage of patients. The principal therapeutic measures can be categorised:

- elimination of toxic agents;
- GAG-substitution/instillation therapy;
- additional drug therapy;
- additional physiotherapeutic and psychotherapeutic treatments;
- hydrodistension of the bladder;
- palliative analgesics; and
- surgery.

Intravesical therapy is one of the mainstays in the treatment of IC. The advantages of intravesical therapy include high drug concentration in the bladder, short dwell times in the bladder, minimal drug absorption, lack of significant systemic side effects and non-interference by renal and liver metabolism.

Evidence supporting the role of the GAG layer in the antibacterial defence and the impermeability of the bladder was demonstrated in animals and humans. This led to the discovery and development of a specific hyaluronic solution for intravesical instillation (Cystistat) for the treatment of various IC conditions. By temporarily replacing the GAG layer in a patient's bladder, intravesical instillation of hyaluronic acid has been shown to provide effective relief of symptoms, including pain, urgency and frequency in a majority of IC patients.<sup>1-10,13-18</sup> Morales et al. found a 71% rate of symptom improvement after four weeks of Cystistat instillation therapy, which was maintained for several months.<sup>1</sup> Since this initial study did not discriminate between early- and end-stage IC, a more effective cure rate of over 80% was observed by Riedl et al. in more than one hundred early stage IC patients with a positive modified potassium, who were more likely to respond to GAG substitution with Cystistat.<sup>10</sup>

### Management of Radiation-induced Cystitis (RIC)

Tumours of the pelvic area are common in both men and women and account for a significant percentage of new cancers. Both external beam radiation therapy (EBRT) and intracavitary brachytherapy have been widely used in the treatment of patients diagnosed with cervical or endometrial carcinoma and their curative value is well documented. It is the standard therapy of patients diagnosed with disease stage IB to IV. While mortality associated with radiation therapy is rare and less frequent than surgical mortality, intestinal and genitourinary complications continue to present serious challenges to urologists, gynaecologists and radiation oncologists. Radiation to the pelvis, particularly in full-dose therapy for pelvic malignancies, can cause detrusor or mucosal injury, which can be manifested at any time during or after initial treatment.

The main acute urinary complication is radiation cystitis, defined as urinary frequency, urinary urgency and aseptic dysuria, with or without haematuria. Approximately 20% of the patients treated with pelvic radiation will develop bladder complications.

Although RIC is treated with a number of therapies, no single consistent effective therapy has been identified. Certain treatments have had serious side effects. Treatments have included oral and intravenous agents, intravesical therapy, selective embolisation of the hypogastric arteries and hyperbaric oxygen therapy.

Positive results have been obtained in the prevention of RIC patients with Cystistat. The use of Cystistat immediately prior to radiotherapy has shown a significant protective effect in patients with pelvic cancers. Cystistat had an excellent rate of success in the prevention of RIC in a study presented at the 2003 American Society of Clinical Oncology Annual Meeting.<sup>11</sup> Another recent study from Greece, presented at the European Society for Therapeutic Radiation and Oncology (ESTRO) conference in October 2004, reported that 60% of patients experienced a significant improvement after three to four week instillations of Cystistat.<sup>18</sup> Cystistat helps to:

- protect the bladder;
- decrease radiation-induced toxicity and risk of infection; and
- improve the overall quality of life for patients.

### Management of Bacterial Cystitis

Cystistat has been used in the prevention of several forms of bacterial cystitis, also known as urinary tract infections (UTIs). A UTI is usually treated with antibiotics; however, widespread use of some antibiotics, especially penicillin and sulfonamide ('sulfa') drugs, has led to an increase in bacterial

resistance. A growing number of patients are also allergic to some, or all, antibiotics.

Cystistat can benefit a high percentage of patients with bacterial cystitis. Recent studies in Europe showed that:

- Cystistat therapy provided a five-fold increase in median time to the recurrence of UTIs from 96 days to 498 days<sup>7</sup>; and
- weekly instillation of Cystistat reduced nosocomial catheter-acquired UTIs from 76.5% to 13.5%.<sup>12</sup>

### Cystistat

Cystistat (sodium hyaluronate, 40mg/50ml) is registered as a medical device in Canada and the EU for the temporary replacement of the GAG layer of the bladder, for the treatment of various forms of cystitis, such as interstitial cystitis, radiation-induced cystitis, cystitis caused by infection, trauma, urolithiasis, urinary retention and neoplasia. Cystistat, administered by bladder instillation, has proved to be well-tolerated through 18 clinical studies involving more than 400 patients. To date, Cystistat is prescribed in over 20 countries around the world and 120,000 treatments of Cystistat have been administered with an exceptional safety profile.<sup>1-18</sup> ■

#### Contact Information

More information regarding patient information, production information, clinical references and abstracts, links to IC patient and medical associations and links to urological, urogynaecological and oncological associations can be found via:

[www.cystistat.com](http://www.cystistat.com)

#### Further Information

Cystistat is patent protected in the US, Canada and Europe.  
 US Patent Nos: 5,591,724; 5,880,108; 5,888,986  
 Canadian Patent No: 2,203,621  
 European Patent No: 0813417

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