NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pentosan polysulfate sodium for treating interstitial cystitis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pentosan polysulfate sodium within its marketing authorisation for treating interstitial cystitis.

Background

Interstitial cystitis (also known as bladder pain syndrome) is a chronic bladder condition characterised by pain, urinary urgency, frequency and nocturia. Symptoms often resemble those of patients with overactive bladder. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. It is not clear what causes interstitial cystitis. In some people with the condition the bladder is inflamed, ulcerated, scarred or stiff. Interstitial cystitis that is characterised by 'Hunner's lesions' (distinctive inflammatory lesions that rupture the bladder lining) is sometimes known as 'classic interstitial cystitis'.[1] The condition can also be characterised by glomerulations (haemorrhages in the bladder wall), although these are not specific to interstitial cystitis. These characteristics can be detected by cystoscopy with hydrodistention. In clinical practice the diagnosis of interstitial cystitis is often made once specific causes such as infection and malignancy have been ruled out.

Interstitial cystitis may affect approximately 300,000 people in England. It is more common in women than men; 90% of people with the condition are women in their fifth and sixth decades of life. Up to 50% of patients with symptoms of interstitial cystitis will have spontaneous resolution in time.[2] Estimates of the proportion of people with the Hunner's lesions subtype range from 5%[3] to 50%[4].

Treatments for bladder pain syndrome are generally aimed at controlling the symptoms, as there is no cure for the condition. Lifestyle changes such as avoiding certain foods and drinks, reducing stress and stopping smoking may help to reduce symptoms. Antihistamine tablets may be prescribed to reduce the inflammation, and painkillers can also be taken.[5;6] Some medicines can be passed directly into the bladder through a catheter to relieve symptoms.[7] Before the marketing authorisation was granted, pentosan polysulfate sodium was sometimes used off-licence to treat interstitial cystitis with glomerulations or Hunner's lesions. [8]

The technology

Pentosan polysulfate sodium (Elmiron, Bene-Arzneimittel) has a marketing authorisation in the UK for treating 'bladder pain syndrome characterized by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition'. Pentosan polysulfate sodium is taken orally.

Pentosan polysulfate sodium is a semi-synthetic heparin-like glycosaminoglycan which controls cell permeability by preventing irritating solutes from reaching cells coated with it. It is thought to work by binding to and repairing the glycosaminoglycan layer in the deficient mucous of the bladder.

Intervention	Pentosan polysulfate sodium
Population	Adults with interstitial cystitis, characterised by either glomerulations or Hunner's lesions, with moderate to severe pain, urgency, and frequency of micturition.
Comparators	Established clinical management without pentosan polysulfate sodium.
Outcomes	The outcome measures to be considered include: • bladder pain • urinary urgency • urinary frequency • nocturia • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The use of pentosan polysulfate sodium is conditional on the presence of either glomerulations or Hunner's lesions. The economic modelling should include the costs associated with diagnostic testing for glomerulations or Hunner's lesions in people with interstitial cystitis who would not otherwise have been

	tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation of pentosan polysulfate sodium. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: None. Related NICE evidence summary: Interstitial cystitis: oral pentosan polysulfate sodium (2015) NICE evidence summary ESUOM43. Interstitial cystitis: dimethyl sulfoxide bladder instillation (2014). NICE evidence summary ESUOM26. Related Quality Standards: Urinary tract infections in adults (2015). NICE quality standard QS90. Related NICE Pathways: Urological conditions (2017) NICE pathway.
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. • Highly specialist adult gynaecological surgery and urinary surgery services for women (section 58, page 137) • Highly specialist adult urological surgery services for men (section 58A, page 142) Department of Health (2016) NHS Outcomes Framework 2016-2017 Domains 2-5.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for interstitial cystitis? Would pentosan polysulfate sodium be used in addition to established clinical practice?

Have all relevant comparators for pentosan polysulfate sodium been included in the scope?

Are the outcomes listed appropriate? How is response to treatment measured in clinical practice? What outcomes are most important to patients?

Are there any subgroups of people in whom pentosan polysulfate sodium is expected to be more clinically effective and cost effective or other groups that should be examined separately? For example, should people with Hunner's lesions and people with glomerulations be examined separately?

Where do you consider pentosan polysulfate sodium will fit into the existing NICE pathway, Urological conditions?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which pentosan polysulfate sodium is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider pentosan polysulfate sodium to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of pentosan polysulfate sodium can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

[1] International Society for the Study of Bladder Pain Syndrome Hunner Lesion (accessed February 2018)
[2] CHMP Assessment report. Elmiron (2017) (accessed February 2018)
[3] Interstitial Cystitis Association Hunner's Ulcers (accessed February 2018)
[4] International Society for the Study of Bladder Pain Syndrome Hunner Lesion (accessed Febraruy 2018)
[5] European Association of Urology (2015) Chronic Pelvic Pain guidelines (accessed February 2018)
[6] Royal College of Obstetricians and Gynaecologists/British Society of Urogynaecology (2016) Management of Bladder Pain Syndrome Green top guideline No. 70 (accessed February 2018)
[7] NHS Choices Interstitial Cystitis (accessed February 2018)
[8] UK Medicines Information (2011) Oral Pentosan for Painful Bladder Syndrome/Interstitial Cystitis: Unlicensed and Off-label Medicines Reports Number 2 (accessed February 2018)