Interstitial cystitis: oral pentosan polysulfate sodium

Evidence summary
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Key points from the evidence

The content of this evidence summary was up-to-date in April 2015. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

Summary

A randomised controlled trial (RCT) published in 2014 found no statistically significant difference between pentosan polysulfate sodium (pentosan) and placebo for the treatment of pain, urinary urgency, frequency and nocturia in people with the chronic bladder condition interstitial cystitis. A meta-analysis of older RCTs that used inconsistent methods for assessing symptoms found that pentosan was more effective than placebo in reducing some symptoms of interstitial cystitis. There are limited data comparing pentosan to other active treatments for interstitial cystitis.

Regulatory status: unlicensed. This topic was prioritised because there was a high volume of requests from the NHS.
<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Safety</th>
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<tr>
<td>• A recent 24-week RCT (n=369) found no statistically significant difference between pentosan and placebo using a validated questionnaire that assesses pain, urinary urgency, frequency and nocturia.</td>
<td>• Adverse events reported by people taking pentosan in clinical trials include diarrhoea, headache, nausea, rash, alopecia and rectal bleeding.</td>
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<td>• A meta-analysis of 4 older RCTs found pentosan improved pain (n=398), urinary urgency (n=306) and frequency (n=160) more than placebo. However, improvements in these symptoms were not seen in all of the individual studies. There was no statistically significant difference in nocturia between pentosan and placebo (n=106). The trials included in the meta-analysis used inconsistent and non-validated methods for assessing symptoms.</td>
<td>• The FDA label for pentosan (Elmiron, Janssen) advises people undergoing invasive procedures or having signs or symptoms of underlying coagulopathy or other increased risk of bleeding should be evaluated for haemorrhage.</td>
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<tr>
<td>• Differences in inclusion criteria and how symptoms were assessed may explain the inconsistent results observed in the clinical trials.</td>
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</tbody>
</table>
Patient factors

- The FDA label for Elmiron recommends people taking pentosan should be reassessed after 3 months, and if improvement has not occurred and if limiting adverse events are not present, treatment may be continued for another 3 months. The clinical value and risks of continuing treatment in people whose pain has not improved by 6 months is not known.

- The FDA label for Elmiron advises that people taking pentosan should be reminded that pentosan has a weak anticoagulant effect; this may increase bleeding times.

Resource implications

- No price is listed for pentosan and the cost will differ depending on the source. The NHS prescription cost analysis for England 2013 reports that the mean cost of pentosan polysulfate sodium 100 mg capsules was £487.14 per item, and the mean quantity per item was 117. This equates to approximately £4.16 per capsule, or £374.40 for 30 days treatment (100 mg 3 times daily).

- The 30-day cost of amitriptyline at dose of 10 mg to 150 mg daily is £1.13 to £3.70 (Drug Tariff March 2015).

- The 30-day cost of cimetidine at a dose of 400 mg twice daily is £1.82 (Drug Tariff March 2015).

- The 30-day cost of ciclosporin at a dose of 100 mg twice a day is £145.14 (MIMS March 2015).

Introduction and current guidance

Interstitial cystitis (also referred to as bladder pain syndrome or chronic pelvic pain syndrome) is a chronic bladder condition characterised by pain, urinary urgency, frequency and nocturia. In clinical practice the diagnosis of interstitial cystitis is often made once specific causes such as infection and malignancy have been ruled out.

There is no NICE guidance on interstitial cystitis.

Guidelines produced by the European Association of Urology (2015) make recommendations on a number of treatments for interstitial cystitis, including patient education, self-care and behaviour modification, manual physical therapy techniques, multimodal pain management approaches, oral drugs and intravesical treatments.
Product overview

Pentosan polysulfate sodium (pentosan) is a low molecular weight heparin-like compound with anticoagulant and fibrinolytic effects. The mechanism of action of pentosan in interstitial cystitis is unknown; it may act as a buffer to control cell permeability preventing irritating solutes in the urine from reaching the cells (FDA label for Elmiron, Janssen).

Pentosan is not licensed in the UK. Pentosan is licensed in other countries, including the USA, for the relief of bladder pain or discomfort associated with interstitial cystitis.

Evidence review

- A double-blind, randomised controlled trial (RCT, n=369) in adults aged 18 or over with interstitial cystitis found no statistically significant difference between pentosan 100 mg 3 times daily and placebo using the Interstitial Cystitis Symptom Index (ICSI), a validated patient questionnaire covering pain, urinary urgency, frequency and nocturia (Nickel et al. 2014). The study was underpowered, randomising only 369 of the required 645 participants. Slow enrolment of participants and an interim analysis of data prompted early termination of the study.

- A meta-analysis included 4 RCTs (n=448) comparing pentosan with placebo in adults (Hwang et al. 1997). The meta-analysis found pentosan statistically significantly improved symptoms of pain, urinary urgency and frequency compared with placebo. There was no statistically significant difference between pentosan and placebo for improvements in nocturia. However, results from the individual studies included in the meta-analysis were inconsistent, with some trials finding no statistically significant difference between pentosan and placebo for these outcomes. The trials included in the meta-analysis used a number of different outcome measures, did not use validated tools to measure responses and some trials used multiple methods to assess a single symptom.

- Differences in inclusion criteria and how symptoms were assessed may explain the inconsistent results seen in the published placebo-controlled trials involving pentosan.

- Trials comparing pentosan with other active treatments are limited. A 6-month, randomised, unblinded trial (n=64) found that after 6 months treatment, a 50% reduction in micturition
frequency was achieved in 11 out of 32 people (34.3%) taking ciclosporin, and no people taking pentosan (p<0.001). More people taking ciclosporin reported adverse events compared with those taking pentosan; 94% compared with 56% (Sairanen et al. 2005).

- A 32-week, randomised, double-blind, dose-ranging study compared 3 different doses of pentosan; 100 mg, 200 mg and 300 mg 3 times daily. At the end of study period the ICSI score for each dose had statistically significantly improved from baseline, although there was no placebo arm for comparison. There was no statistically significant difference in ICSI score between the 3 different doses. The trial was underpowered; only 230 (60.5%) of the 380 participants completed the study.

- The study found diarrhoea and rectal bleeding were the only adverse events that were dose-dependent. Statistically significantly more people taking the highest dose discontinued treatment due to adverse events compared with people taking the lowest dose (Nickel et al. 2005).

- Pentosan is a weak anticoagulant. The FDA label for Elmiron (Janssen) advises that people undergoing invasive procedures, those who may have signs or symptoms of underlying coagulopathy and people with other increased risk of bleeding (for example due to other treatments) should be evaluated for haemorrhage.

- Adverse events reported by people taking pentosan in clinical trials include diarrhoea, headache, nausea, rash, alopecia and rectal bleeding.

Full text of evidence review.

**Context and estimated impact for the NHS**

No estimate of the current use of pentosan for interstitial cystitis was identified. No price is listed for pentosan and the cost will differ depending on the source. The NHS prescription cost analysis for England 2013 reports that the mean cost of pentosan polysulfate sodium 100 mg capsules was £487.14 per item, and the mean quantity per item was 117. This equates to approximately £4.16 per capsule, or £374.40 for 30 days treatment (100 mg 3 times daily). In 2013, 400 items of pentosan polysulfate sodium 100 mg were dispensed at a net cost of £214,300. It is not known for which indications these items were prescribed.

Full text of context and estimated impact for the NHS.
Information for the public

A plain English summary is available on the NICE website. This sets out the main points from the evidence summary in non-technical language and may be especially helpful for people with interstitial cystitis who are thinking about trying pentosan.

About this evidence summary

‘Evidence summaries: unlicensed or off-label medicines’ summarise the published evidence for selected unlicensed or off-label medicines that are considered to be of significance to the NHS, where there are no clinically appropriate licensed alternatives. The summaries provide information for clinicians and patients to inform their decision-making and support the construction and updating of local formularies.

The summaries support decision-making on the use of an unlicensed or off-label medicine for an individual patient, where there are good clinical reasons for its use, usually when there is no licensed medicine for the condition requiring treatment, or the licensed medicine is not appropriate for that individual.

The strengths and weaknesses of the relevant evidence are critically reviewed within this summary, but this summary is not NICE guidance.

Full evidence summary

Introduction and current guidance

Interstitial cystitis (also referred to as chronic pelvic pain syndrome or bladder pain syndrome) is a chronic bladder condition characterised by pain, urinary urgency, frequency and nocturia. Interstitial cystitis is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. The condition is 10 times more common in women than men.

There is no NICE guidance on interstitial cystitis.

The European Association of Urology Guidelines on Chronic Pelvic Pain (2015) recommends oral pentosan as a treatment option, alongside other oral drugs (including amitriptyline, cimetidine and ciclosporin), invasive treatments, and behavioural, physical and psychological techniques.

There are no licensed preparations available in the UK for the treatment of interstitial cystitis.
An Evidence Summary Unlicensed Off-label Medicine Interstitial cystitis: dimethyl sulfoxide bladder instillation was published in February 2014.

Diagnosis

Interstitial cystitis is a poorly defined clinical condition without standardised diagnostic criteria. Diagnostic criteria suggested by the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) in 1988 required people to have pain or urgency, and either glomerulations or a Hunner's lesion (an erythematous lesion) on cystoscopic examination. These criteria were designed to standardise participants recruited to clinical trials, but there is controversy as to their usefulness for routine clinical diagnosis. More recent diagnostic criteria proposed by the European Society for the Study of Interstitial Cystitis (ESSIC) suggest that diagnosis should be based on symptoms only, with cystoscopy results used to define subtypes of the condition (van de Merwe et al. 2008). In many cases the diagnosis of interstitial cystitis is made by exclusion, once specific causes such as infection and malignancy have been ruled out (Dawson and Jamison 2007).

Product overview

Drug action

Pentosan polysulfate sodium (pentosan) is a low molecular weight heparin-like compound. It has anticoagulant and fibrinolytic effects. The mechanism of action of pentosan in interstitial cystitis is not known; it may act as a buffer to control cell permeability preventing irritating solutes in the urine from reaching the cells.

Regulatory status

Pentosan is not licensed in the UK. However, it is licensed in other countries, including the USA, for interstitial cystitis.

Pentosan polysulfate sodium 100 mg capsules are licensed in the USA for the relief of bladder pain or discomfort associated with interstitial cystitis. The FDA label for Elmiron (Janssen) recommends a dose of 100 mg 3 times daily, advising that capsules should be taken with water at least 1 hour before meals or 2 hours after meals.

The FDA label for Elmiron (Janssen) states that the safety and effectiveness of pentosan in people younger than 16 years has not been established.
The FDA label for Elmiron (Janssen) advises that people taking pentosan should be reassessed after 3 months, and if improvement has not occurred and if limiting adverse events are not present, treatment may be continued for another 3 months. The clinical value and risks of continued treatment in people whose pain has not improved by 6 months is not known.

In line with the guidance from the General Medical Council (GMC), it is the responsibility of the prescriber to determine the clinical need of the patient and the suitability of using pentosan as it is not licensed for any indication in the UK.

**Cost**

Because pentosan is not licensed in the UK, no price could be obtained from standard published sources (Drug Tariff or MIMS) and the cost will differ depending on the source. The NHS prescription cost analysis for England 2013 reports that the mean cost of pentosan polysulfate sodium 100 mg capsules was £487.14 per item, and the mean quantity per item was 117. This equates to approximately £4.16 per capsule, or £374.40 for 30 days treatment (100 mg 3 times daily).

**Evidence review**

This evidence summary is based on a randomised controlled trial (RCT) (Nickel et al. 2014) comparing pentosan with placebo, and a meta-analysis of 4 older RCTs also comparing pentosan with placebo (Hwang et al. 1997). The evidence summary also discusses 1 RCT which compared pentosan with ciclosporin (Sairanen et al. 2005). A randomised, uncontrolled dose-ranging study is also briefly discussed (Nickel et al. 2005). Additional safety information is taken from an open-label study (Hanno 1997).

**Clinical effectiveness**

**Pentosan compared with placebo**

Nickel et al. 2014

This double-blind, randomised controlled trial compared the efficacy and safety of two doses of pentosan with placebo. The trial was conducted across 67 study sites in the USA and Canada, recruiting adults aged 18 or over with interstitial cystitis (n=369, mean age 44, 90% female). Participants were required to have an average of at least 10 voids per day, with 1 or more occurring during the night. Participants were required to score 8 or more on the validated O’Leary-Sant Interstitial Cystitis Symptom Index (ICSI), with a score greater than 0 on each of the component
items. The ICSI is a 4 item self-administered questionnaire covering bladder pain, urinary urgency, frequency and nocturia. Each question in the ICSI is answered using a 0 to 5 rating scale. The sum of these ratings is the ICSI score (range 0 to 20); a higher score indicates worse symptoms. Participants were not required to have cystoscopy results confirming diagnosis.

Participants were randomised to pentosan 100 mg 3 times daily (the licensed dose in the USA), pentosan 100 mg once daily or placebo. It is unclear if allocation was concealed. The primary endpoint was the number of people having at least a 30% reduction in ICSI score from baseline to week 24. For people who withdrew from the study before week 24 the last observed data were carried to the end point for analysis. Secondary endpoints included the number of participants with a reduction of 4 points or more in the ICSI and Patient’s Overall Rating of Improvement of Symptoms (PORIS) score (which measured pain, urgency and overall change).

Slow enrolment of participants and an interim analysis of data prompted early termination of the study.

The investigators found no statistically significant difference between pentosan (at either dose) and placebo for the primary endpoint, with a responder rate of 40.7% (48 out of 118) in the placebo arm, 39.8% (51 out of 128) in the pentosan 100 mg daily arm and 42.6% (52 out of 122) in the pentosan 100 mg 3 times daily arm, p values not reported.

The authors reported that there was no statistically significant difference between treatment arms for all secondary endpoints, including number of people with a 4 point or greater improvement in ICSI score and for symptoms reported using the PORIS scale, p values not reported.

Hwang et al. 1997

A meta-analysis which assessed the efficacy of pentosan for interstitial cystitis, included 4 RCTs (n=448, mean age 44 years, 93% women), that compared pentosan with placebo. The meta-analysis included randomised, placebo-controlled trials that lasted for at least 8 weeks (duration of included studies ranged from 3 to 6 months), used a pentosan dose of 300 mg daily or higher, involving adults with 1 or more symptoms including pain, urgency, frequency and nocturia, with symptoms lasting at least 12 months.

All 4 studies compared pentosan to placebo, with 2 studies using the dose licensed in the USA, 100 mg 3 times daily (Mulholland et al. 1990, Parsons et al. 1993), 1 study used 200 mg twice daily (Holm-Bentzen et al. 1987) and 1 study was conducted in 2 medical centres, with one institution using the licensed dose and the other using 200 mg twice daily (Parsons and Mulholland 1987).
Treatment success was defined as a decrease in a symptom by 50% or more. Data on the number of people reporting success for each variable (pain, urgency, frequency and nocturia) were analysed separately. All studies used patient questionnaires to assess symptomatic improvements, but methods varied between studies. Patients were either asked to score improvements in symptoms from "not improved at all" (0%), through to "moderately improved" (50%) and "completely cured" (100%), or asked to score symptoms on a 5 or 6 point scale, with higher numbers for worse symptoms. It is not clear from the published trial reports how the different symptoms were classified or described to participants. Three of the studies asked people to report their level of 'pain' (Parsons and Mulholland 1987, Mulholland et al. 1990, Parsons et al. 1993), and one study assessed 'pain' and 'dysuria' as separate symptoms (Holm-Bentzen et al. 1987).

Data was available from all 4 studies on pain (n=398), with 76 out of 204 people in the pentosan group reporting improvement in pain scores of 50% or more, compared with 41 out of 194 people taking placebo (percentage difference 16.6%, 95% confidence interval [CI] 8.0 to 25.2, number needed to treat [NNT]=7). Results from the individual studies were inconsistent, with 2 studies reporting no statistically significant difference between pentosan and placebo for pain (Holm-Bentzen et al. 1987, Mulholland et al. 1990).

Three studies reported on urgency (n=306), with 45 out of 157 people taking pentosan reporting improvements of 50% or more, compared with 23 out of 149 people who received placebo (percentage difference 12.9%, 95% CI 1.0 to 25.0, NNT=8). Although the difference between pentosan and placebo for urgency was statistically significant in the meta-analysis, the results for each individual trial were not statistically significant (Parsons and Mulholland 1987, Mulholland et al. 1990, Parsons et al. 1993).

Results from 2 studies (n=160, Holm-Bentzen et al. 1987, Parsons and Mulholland 1987) found 43 out of 83 people on pentosan reported improvements of 50% or more in urinary frequency, compared with 27 out of 77 in the placebo group (percentage difference 16.7%, 95% CI 2.3 to 31.1, NNT=6). Although the combined trial data showed pentosan improved urinary frequency compared with placebo, the results from the individual studies found no statistically significant difference between pentosan and placebo.

Only 1 study (n=106) provided results for nocturia (Holm-Bentzen et al. 1987), which found no statistically significant difference between pentosan and placebo (48.1% compared to 49.1% for placebo, p=0.887).
Nickel et al. 2005

A randomised, double-blind trial compared 3 doses of pentosan, evaluating efficacy and safety. The study did not have a placebo arm.

The study recruited adults with interstitial cystitis, determined by a history of symptoms (bladder pain, urinary urgency, frequency, and nocturia) for at least 6 months or a positive cystoscopic examination combined with bladder pain and urgency. A sample size of 309 participants was required to detect with 80% power a difference of 1.0 point in the ICSI score. Participants were randomised to pentosan 100 mg, 200 mg or 300 mg 3 times daily for 32 weeks. The primary endpoint was the ICSI score at 32 weeks. A total of 380 people were randomised, 90% of whom were female, mean age 44.2 years. At the end of study period there was no statistically significant difference in ICSI score between the 3 different doses of pentosan. The ICSI score for each dose had statistically significantly improved from baseline (from 11.2 to 8.2 in the pentosan 100 mg 3 times daily group, p<0.001), although there was no placebo arm to compare this change with. The authors reported that the time to response was not dose dependent. Of the 380 participants enrolled only 230 people (60.5%) completed the study, causing the trial to be underpowered.

Sairanen et al. 2005

The efficacy and safety of pentosan was compared with ciclosporin in a 6 month randomised trial involving people with interstitial cystitis that had been diagnosed from symptoms and cystoscopy results, meeting NIDDK diagnosis criteria (n=64; mean age 58 years; 82.8% female). Patients were randomised to pentosan 100 mg 3 times daily or ciclosporin 1.5 mg/kg twice daily. There was no placebo arm. The primary outcome measure was a 50% reduction in daily micturition frequency from baseline. Secondary endpoints included ICSI score, maximal bladder capacity and number of nocturia episodes. After 6 months treatment a 50% reduction in micturition frequency was achieved in 11 out of 32 people (34.3%) taking ciclosporin (mean reduction 6.7 ± 4.7 [standard deviation]) and no people (0%) receiving pentosan (mean reduction 2.0 ± 5.1, p<0.001). Statistically significantly greater improvements for all secondary endpoints were observed in the ciclosporin group compared to pentosan. However, although ciclosporin was found to be more effective than pentosan, participants receiving ciclosporin had more adverse events compared with those taking pentosan.
Safety and tolerability

The FDA label for Elmiron (Janssen) 100 mg (pentosan polysulfate sodium) advises that pentosan is a weak anticoagulant, with 1/15 the activity of heparin. At the licensed dose of 100 mg 3 times daily rectal haemorrhage was reported as an adverse event in 6.3% of people taking pentosan. Bleeding complications of ecchymosis, epistaxis, and gum haemorrhage have been reported. The FDA label for Elmiron (Janssen) advises that people undergoing invasive procedures or having signs/symptoms of underlying coagulopathy or other increased risk of bleeding (due to other therapies such as coumarin anticoagulants, heparin, tissue plasminogen activator, streptokinase, high dose aspirin, or nonsteroidal anti-inflammatory drugs) should be evaluated for haemorrhage. People with diseases such as aneurysms, thrombocytopenia, haemophilia, gastrointestinal ulcerations, polyps, or diverticula should be carefully evaluated before starting pentosan.

In Nickel et al. 2014 the most common adverse events were bladder pain, headache and nausea, occurring in 38.5%, 11.5% and 9.8% people respectively in the pentosan 100 mg 3 times daily group, compared with 32.2%, 13.6% and 7.6% in the placebo group. Adverse events (mostly gastrointestinal) led to the withdrawal of 12 out of 118 people (10.2%) in the placebo group, 14 out of 122 people (11.5%) in the pentosan 100 mg 3 times daily group and 17 out of 128 people (13.3%) in the pentosan 100 mg once daily group. Serious adverse events were only reported in the placebo group (in 4 people) only. No statistical analysis was presented.

Nickel et al. 2005 reported that most adverse events across the 3 doses of pentosan (100 mg, 200 mg and 300 mg 3 times daily) were mild and resolved without intervention. Across the different doses the most common adverse events were diarrhoea (25.3%), headache (18.2%), nausea (15.0%), pelvic pain (12.9%) and abdominal pain (12.6%). Diarrhoea and rectal bleeding were the only dose-dependent adverse events, with statistically significantly higher rates in the 300 mg 3 times daily group. Differences between doses were reported as not statistically significant for all other adverse events. Statistically significantly more people taking the 300 mg 3 times daily dose discontinued treatment due to adverse events compared with the 100 mg 3 times daily dose (30.7% compared with 18.0%, p<0.05).

The meta-analysis (Hwang et al. 1997) did not analyse safety data from the studies. Of the RCTs included in the meta-analysis Parsons and Mulholland 1987 reported 1 adverse event among those participants who completed the study (skin rash), although this was a cross-over study and the authors do not state if the adverse event occurred during the pentosan or placebo phase. Holm-Bentzen et al. 1987 reported that 5 people who received pentosan experienced peripheral oedema and 1 participant reported a skin rash. Mulholland et al. 1990 stated that 1 person in the pentosan group and 2 people in the placebo group discontinued treatment due to adverse reactions. Parsons
et al. 1993 reported that 7 people (9%) receiving pentosan experienced 12 adverse events and 10 people (14%) taking placebo experienced 19 adverse events. The only adverse events reported in more than one person were nausea, diarrhoea and vomiting, and these were more common in the placebo group compared to the pentosan group (7 events compared to 3 events).

In Hanno 1997 the safety of pentosan was assessed in an open-label study involving 2809 adults with interstitial cystitis, diagnosed from symptoms and cystoscopy results. The duration of treatment varied between participants, with some discontinuing treatment within the first 3 months and others continuing treatment for more than 60 months. The most frequently occurring adverse effects were alopecia (3.9%), diarrhoea (3.7%), nausea (3.7%), headache (2.9%) and rash (2.5%). The study had a high discontinuation rate, with 1239 out of 2809 participants (44.1%) dropping out during the first 3 months. The authors reported that of the 1974 participants giving a reason for discontinuing the study, 432 people (21.8%) did so because of an adverse event.

In Sairanen et al. 2005 adverse events were more common in the ciclosporin group, with 30 out of 32 participants (94%) experiencing an adverse event, compared with 18 out of 32 (56%) in the pentosan arm. Significant adverse events were reported by 9.4% of people taking ciclosporin, compared with 3.0% in the pentosan group. No statistical analysis was presented. The most common adverse events in the pentosan group were gastrointestinal disturbances, fatigue, headache and colic pelvic pain, while in the ciclosporin arm mild to moderate adverse events included hair growth, gingival pain and hyperplasia, paraesthesias, abdominal pain, flushing, muscle pain and shaking.

Evidence strengths and limitations

The studies included in this evidence summary have given conflicting results about the effectiveness of pentosan for the treatment of interstitial cystitis. Variation in diagnostic criteria for interstitial cystitis makes it difficult to compare studies. Early studies, such as those included in Hwang et al. 1997, enrolled people with the traditional NIDDK diagnosis of interstitial cystitis, namely people with pain or urgency symptoms and positive cystoscopy results (presence of glomerulations or a Hunner’s lesion). In contrast, more recent studies (Nickel et al. 2005 and Nickel et al. 2014) did not require positive cystoscopy findings for inclusion.

The most recently published RCT investigating the efficacy of pentosan (Nickel et al. 2014) was a well-designed study using a validated patient-oriented outcome measure. However the study was underpowered, randomising only 369 of the required 645 participants. There was also a high drop-out rate in each arm of the trial; 163 of the 369 participants did not complete the study. A high
drop-out rate was also a limitation of the 32-week dose-ranging study conducted by Nickel et al. (2005), with 150 out of 380 participants (39.5%) not completing the study.

The outcomes reported for most of the included studies were patient-oriented, although the use of several different endpoints makes it difficult to compare treatments across different studies. The validated O’Leary-Sant Interstitial Cystitis Symptom Index (ICSI) was used in two RCTs (Nickel et al. 2005 and Nickel et al. 2014). The older RCTs included in the meta-analysis (Hwang et al. 1997) used a number of different outcome measures, did not use a validated tool to measure response and some trials used multiple methods to assess a single symptom. In addition to this, the trials included in the meta-analysis were small (n=62 to 148), and key aspects of the trial methodology (for example methods of allocation concealment) were not described in the published papers.

**Context and estimated impact for the NHS**

**Cost effectiveness**

No studies assessing the cost effectiveness of pentosan for interstitial cystitis were identified.

The table below gives the costs of alternative oral treatment options for interstitial cystitis based on treatments recommended in the European Association of Urology Guidelines on Chronic Pelvic Pain (2015). There are no licensed preparations available in the UK for the treatment of interstitial cystitis.

**Table 1 Costs of alternative oral treatment options for treating interstitial cystitis**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Usual dose</th>
<th>Estimated cost for 30 days treatment (excluding VAT)</th>
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<tr>
<td>Pentosan polysulfate</td>
<td>100 mg 3 times daily</td>
<td>£374.40b</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10 mg to 150 mg once a dayc</td>
<td>£1.13 to £3.70d</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>400 mg twice a daye</td>
<td>£1.82d</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>100 mg twice a dayf</td>
<td>£145.14g</td>
</tr>
</tbody>
</table>
Doses taken from the summaries of product characteristics, trial data and consensus expert opinion. None of these drugs is licensed specifically for treatment of interstitial cystitis and use would be off-label or, in the case of pentosan, unlicensed. The doses shown do not represent the full range that can be used and they do not imply therapeutic equivalence.

Price based on estimate from the NHS prescription cost analysis for England 2013, which reported that pentosan polysulfate sodium 100 mg capsules cost £487.14 per item; mean quantity per item was 117. This equates to approximately £4.16 per capsule, or £374.40 for 30 days treatment.


Price based on Drug Tariff March 2015.

Dose used in Thilagarajah et al. 2001.

Dose used in Sairanen et al. 2005.

Price based on MIMS March 2015.

Current drug usage

The NHS prescription cost analysis for England 2013 reports that approximately 400 community prescriptions for pentosan were dispensed in 2013, costing around £214,300 (net ingredient cost). The indications for these prescriptions are not provided. These data do not include hospital prescriptions.

Information for the public

A plain English summary is available on the NICE website. This sets out the main points from the evidence summary in non-technical language and may be especially helpful for people with interstitial cystitis who are thinking about trying pentosan.

Relevance to NICE guidance programmes

This use of pentosan is not appropriate for referral for a NICE technology appraisal and is not currently planned into any other work programme.

References


Development of this evidence summary

The integrated process statement sets out the process NICE uses to select topics for the evidence summaries for unlicensed/off-label medicines and how the summaries are developed, quality assured and approved for publication.

Expert advisers

Mr Roland Morley, Consultant Urologist, British Association of Urological Surgeons

Mr William Turner, Consultant Urologist, Cambridge University Hospitals NHS Foundation Trust

Declarations of interest

No relevant interests declared

About this evidence summary

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The summaries support decision-making on the use of an unlicensed or off-label medicine for an individual patient, where there are good clinical reasons for its use, usually when there is no licensed medicine for the condition requiring treatment, or the licensed medicine is not appropriate for that individual.

The strengths and weaknesses of the relevant evidence are critically reviewed within this summary, but this summary is not NICE guidance.

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Interstitial cystitis: oral pentosan polysulfate sodium (ESUOM43)