NICE National Institute for Health and Care Excellence

NICE guidance

Pentosan polysulfate sodium for treating bladder pain syndrome

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces ESUOM43.

1 Recommendations

1.1 Pentosan polysulfate sodium is recommended as an option for treating bladder pain syndrome with glomerulations or Hunner's lesions in adults with urinary urgency and frequency, and moderate to severe pain, only if:

- their condition has not responded to an adequate trial of standard oral treatments
- it is not offered in combination with bladder instillations
- any previous treatment with bladder instillations was not stopped because of lack of response
- it is used in secondary care and
- the company provides pentosan polysulfate sodium according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with pentosan polysulfate sodium that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Bladder pain syndrome causes extreme pain and severely affects quality of life. It is challenging to treat and there is an unmet need for other treatments. It is currently managed with oral treatments, then bladder instillations if symptoms don't improve. Pentosan polysulfate sodium is an oral treatment.

Clinical trials suggest that pentosan polysulfate sodium may be more effective at relieving pain than placebo. A comparison of clinical trials that includes best supportive care and bladder instillations suggests that pentosan polysulfate sodium may have a modest benefit

over these alternatives. But how much benefit it provides is unclear because these treatments haven't been compared directly. Also, the available evidence is not of high quality.

Pentosan polysulfate sodium is not cost effective compared with best supportive care. But the most plausible cost-effectiveness estimates for pentosan polysulfate sodium compared with bladder instillations are likely to be a cost-effective use of NHS resources. So, it is recommended for a defined population.

2 Information about pentosan polysulfate sodium

Marketing authorisation indication

2.1 Pentosan polysulfate sodium (Elmiron, Consilient Health) has a marketing authorisation for treating 'bladder pain syndrome characterised by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition'.

Dosage in the marketing authorisation

2.2 The recommended dosage is 300 mg/day taken as 1 × 100-mg capsule orally 3 times daily.

2.3 Treatment is stopped if no improvement is reached 6 months after starting treatment. In people whose condition responds, treatment should be continued as long as the response is maintained. Response to treatment should be reassessed every 6 months.

Price

2.4 A pack of 90 capsules (100 mg each) costs £450.

2.5 The company has a commercial arrangement. This makes pentosan polysulfate sodium available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by Consilient Health, a review of this submission by the evidence review group (ERG), and the technical report developed through engagement with stakeholders. See the committee papers for full details of the evidence.

The appraisal committee was aware that several issues were resolved during the technical engagement stage, and agreed that these were acceptable:

- using a lifetime time horizon in the economic model (issue 2, see technical report page 21)
- assuming response rates to best supportive care did not recede over time in the model (issue 3, see technical report pages 7 to 10)
- using the ERG's updated survival analysis that censored those who died and used a log-normal extrapolation (issue 4, see technical report page 21)
- assuming utility scores and costs returned to baseline in the model for people whose condition did not respond to treatment who moved on to best supportive care (issue 6, see technical report pages 21 to 22).

  It recognised that there were remaining areas of uncertainty associated with the analyses presented (see technical report, table 2, pages 19 to 20), and took these into account in its decision making.

The condition

Bladder pain syndrome is challenging to manage and affects quality of life

3.1 The clinical experts explained that bladder pain syndrome is a chronic bladder condition characterised by pain, urinary urgency, frequency and getting up at night to pass urine. The patient expert explained that people with bladder pain

syndrome need the toilet up to 60 times a day and that some people had considered suicide because of the pain. Treatments generally aim to control the symptoms because there is no cure for the condition. The committee concluded that bladder pain syndrome is incurable, very challenging to manage and causes extreme pain, which severely affects quality of life.

Clinical management

The relevant population is people with bladder pain syndrome and either glomerulations or Hunner's lesions

3.2 The clinical experts explained that bladder pain syndrome may affect approximately 400,000 people in the UK but only around 10% of these will present for treatment. The committee acknowledged that within the broader bladder pain syndrome population are people who also have glomerulations or Hunner's lesions. The marketing authorisation for pentosan polysulfate sodium is for treating 'bladder pain syndrome characterised by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition'. The committee considered that this was the relevant population for the appraisal.

There is an unmet need for effective treatment options

3.3 Treatment options for people with bladder pain syndrome and either glomerulations or Hunner's lesions include:

- oral treatments (such as amitriptyline, gabapentin, pregabalin, paracetamol, non-steroidal anti-inflammatory drugs, hydroxyzine, cimetidine and ranitidine) and
- bladder instillations (a plastic tube inserted into the bladder to administer liquid medication).

The patient expert stated that there were few treatment options and people often need multiple treatments to manage the symptoms. The clinical experts

explained that bladder instillations were invasive and can cause adverse effects. The patient and clinical experts explained that pentosan polysulfate sodium may also affect quality of life because it has to be taken 3 times a day on an empty stomach, which affects mealtimes. The committee concluded that there was an unmet need for effective treatment options that can be used instead of invasive bladder instillations.

There is substantial variability in the treatment pathway

3.4 The clinical experts explained that the treatment pathway for bladder pain syndrome can vary substantially between services across the country. They added that the condition is difficult to diagnose and the presence of glomerulations is not specific to bladder pain syndrome. Services use international guidelines to guide clinical management and the recommendations for treating the condition vary. The company noted that bladder pain syndrome is initially treated with oral medication (see section 3.3). If glomerulations or Hunner's lesions are found, then people can continue to have oral treatments as best supportive care or be offered bladder instillations. The patient experts explained that not all treatments are available in all areas of the country. Treatments typically depend on where a person lives and what is offered at their local hospital rather than what is best for their condition. The company and clinical experts stated that pentosan polysulfate sodium would only be used in secondary care. The committee recognised that there is substantial variability in the clinical management of bladder pain syndrome and the treatment pathway is poorly defined. However, the committee agreed that pentosan polysulfate sodium would only be available as a treatment option in secondary care.

The comparison with bladder instillations is relevant for decision making

3.5 The company submitted analyses comparing pentosan polysulfate sodium with bladder instillations. At the second committee meeting, the company said that it was positioning pentosan polysulfate sodium as an alternative to bladder instillations. Bladder instillations are offered to people who can tolerate them. The

clinical experts explained that other treatment options for the condition are available. They noted that laser surgery for Hunner's lesions can be considered at any point in the treatment pathway. Also, botulinum toxin type A and sacral neuromodulation are generally used in research and not routine clinical practice. The clinical experts explained that, if available, pentosan polysulfate sodium would be tried before bladder instillations. The committee recognised that pentosan polysulfate sodium could be offered at different points in the treatment pathway but would tend to be used before bladder instillations. Considering the information from the clinical experts, the committee agreed that bladder instillations were a standard clinical management option for this condition and were a relevant comparator.

The comparison with best supportive care is also relevant for decision making

3.6 The company's submission included analyses comparing pentosan polysulfate sodium with best supportive care (which is the continuation of oral medication). However, after consultation the company stated that it did not consider pentosan polysulfate sodium to be an alternative to best supportive care. At the first committee meeting, the clinical experts advised that best supportive care is offered to people who can't tolerate bladder instillations, or if bladder instillations are unsuitable for them. They highlighted that some people would choose best supportive care because bladder instillations are invasive. The clinical experts estimated that bladder instillations would not be suitable for less than 5% of patients. The committee recognised that the proportion of people who would have best supportive care instead of bladder instillations was low. However, it considered that pentosan polysulfate sodium would be an alternative treatment option for this group of people. Because of this, the committee concluded that best supportive care was still a relevant comparator for this limited population.

Clinical effectiveness

There is substantial uncertainty in the pentosan polysulfate sodium evidence

3.7 The company's clinical effectiveness evidence came from 4 randomised controlled trials comparing pentosan polysulfate sodium with placebo in people with bladder pain syndrome and either glomerulations or Hunner's lesions. The trials were published between 1987 and 2003. The ERG noted that:

- 3 of the trials were of good methodological quality but the other trial should be interpreted with caution because of uncertainty about allocation concealment and numbers of patients withdrawing from treatment
- sample sizes were not calculated for 3 of the trials and the target sample size for the other trial was not met
- the author was common to all 4 trials and there were no independent studies validating the results
- the definition of the primary outcome used in the company's model varied and
- follow-up times varied between all trials.

The committee concluded that the company's evidence for pentosan polysulfate sodium was based on the most relevant trials available but acknowledged the limitations of the trials. It considered that there was substantial uncertainty in the clinical effectiveness evidence.

There are substantial uncertainties in determining the relative treatment effect using an indirect treatment comparison

3.8 To compare pentosan polysulfate sodium with bladder instillations, the company used an indirect treatment comparison. Both the company and the ERG acknowledged that this was necessary, but agreed it was challenging because of:

- Differences in trial populations: Uracyst was the only bladder instillation suitable for indirect comparison with pentosan polysulfate sodium via placebo. The pentosan polysulfate sodium trials were in people with interstitial cystitis or bladder pain syndrome who had Hunner's lesions or glomerulations or both. But the Uracyst trials were in people with the broader bladder pain syndrome.
- Differences in placebos: Pentosan polysulfate sodium was compared with an oral placebo, whereas Uracyst was compared with a placebo instillation.
- Differences in the timings of outcome measurement.
- Differences in the definition of the main outcome (global response assessment).

The company compared meta-analysed data from 2 Uracyst trials with meta-analysed data from 4 pentosan polysulfate sodium trials using the Bucher method of indirect treatment comparison (an adjusted method that retains patients' original randomisation). Response rates to treatment were 33% for pentosan polysulfate sodium compared with 22% for bladder instillations. The ERG considered that the Bucher method did not adequately acknowledge the heterogeneity in treatment effect between the studies. Instead, it proposed using a Bayesian network meta-analysis, which provides a more flexible framework for incorporating and exploring the uncertainties in the evidence. The committee acknowledged that both the Bucher method and Bayesian approach were valid methods of analysis in this setting, but the company's application of the Bucher method did not account for heterogeneity. The committee agreed that there was significant heterogeneity in the treatment effect and therefore concluded that it would prefer a Bayesian network meta-analysis.

The ERG's Bayesian network meta-analysis is an acceptable method for an indirect treatment comparison

3.9 The ERG did a Bayesian network meta-analysis, which showed response rates of 33% for pentosan polysulfate sodium compared with 24% for bladder instillations.

After the technical engagement stage, the company also did a Bayesian network meta-analysis comparing pentosan polysulfate sodium with bladder instillations as a scenario analysis. This showed response rates of 38% for pentosan polysulfate sodium compared with 28% for bladder instillations. The ERG advised that the company's network meta-analysis had methodological limitations because it did not use separate baseline and treatment effects models to estimate absolute response rates. The committee understood that although both the company's and the ERG's approaches had their limitations, the best possible methods should be used for an indirect treatment comparison. At the first meeting, the committee concluded that the ERG's Bayesian network meta-analysis was acceptable because it better characterised the uncertainty in comparing active treatments. After consultation, the company argued that neither method was ideal and so kept the Bucher method in its base-case analysis. The committee agreed that all the indirect treatment comparisons it had seen had limitations. But it considered that it had not heard anything to change its original decision that the ERG's Bayesian network meta-analysis was more acceptable than the company's Bucher method.

It is acceptable to use the 16% response rate to placebo from the pentosan polysulfate sodium trials in the cost-effectiveness analysis

3.10 The company noted that the high response rates (16%) in the placebo arms of the pentosan polysulfate sodium trials did not reflect clinical practice. It considered these high response rates would underestimate the effectiveness of pentosan polysulfate sodium. The ERG noted that the high response rates could be explained by regression to the mean, which would also be present in the intervention arms. The ERG also noted that in the company's model, the absolute difference in treatment effect becomes greater with increasing best supportive care response. This would result in the high response rate in the placebo arm favouring pentosan polysulfate sodium because the company's analysis used relative risks. The company's base-case analysis modelled a 15.8% placebo response rate. The company's Bayesian scenario analysis included the placebo arms of the bladder instillation trials, which gave an 18.9% estimated response rate. The clinical experts explained that real-world evidence may suggest even higher placebo response rates. This is expected because patients with the

condition initially have benefit, but this is not sustained beyond 3 months. The committee acknowledged that the clinical experts' views and the ERG's analysis results (15.5%) were broadly in line with the placebo response rates from the pentosan polysulfate sodium trials (16%). The committee concluded that a 16% response rate to placebo was acceptable to use in the cost-effectiveness analysis, and that the company's base-case analysis was in line with this.

Utilities

Missing data on utility values are not adequately accounted for in the company's model

3.11 In its base-case model, the company applied a utility decrement associated with bladder instillations. The company mapped patient survey data collected in the Sant et al. (2003) trial to EQ-5D data. The company used responses to a question in the survey on the use of bladder instillations in the previous 6 months. The ERG noted that the wording of this survey question was vague. This could have meant that patients who had never had bladder instillations did not answer the question and this was recorded incorrectly as missing data. The ERG's preferred method to account for the missing data was to use multiple imputation (a statistical method used to reduce bias arising from missing data). After consultation, the company outlined that multiple imputation was not appropriate because the missing data were not missing at random. The company also highlighted methodological challenges because the data predicted by the imputation would depend on the data that informed the imputation. The committee understood that there were very few responses from the patient survey about quality of life associated with pentosan polysulfate sodium treatment. The committee concluded that missing data from the patient survey was not adequately accounted for in the company's model.

There is insufficient evidence of a direct link between bladder instillations and urinary tract infections

3.12 After the technical engagement stage, the company provided clinical expert

evidence and a systematic review to support its assumption that bladder instillations are associated with an increase in urinary tract infections (UTIs). The company explained that the evidence showed that people with UTIs have substantially lower quality of life than those without UTIs. It also proposed that UTIs in people with bladder pain syndrome have a bigger impact on quality of life than UTIs in the general population. The ERG noted that the company's model assumed that everyone having bladder instillations would have a UTI and that the associated decrement was modelled for a lifetime. The clinical experts explained that not all people having bladder instillations would get a UTI and although the symptoms may last longer than for the general population these would not continue indefinitely. They also noted that people would have the choice of continuing bladder instillation treatment if they did get a UTI. The company noted that UTIs are only 1 aspect of the decrement associated with bladder instillations. After consultation, the company emphasised the evidence relating to the impact of UTIs on quality of life including the quality of life data reported by Cervigni et al. (2017). The committee considered that the Cervigni study was not generalisable to the population covered by the pentosan polysulfate sodium marketing authorisation. This was because the study included a trial population who were not covered by the marketing authorisation (pentosan polysulfate sodium was used as initial treatment for some patients and for others, pentosan polysulfate sodium treatment had already failed before), which introduced some uncertainty into the analyses. The study was based on Italian EQ-5D valuation and the values in the study didn't correspond with response to treatment. The committee considered that it had not seen any new information about the duration of UTIs or the proportion of patients who had UTIs. The committee concluded that there was insufficient evidence to assume a direct link between bladder instillations and UTIs and that any associated decrement was likely to be short-lived.

It is not appropriate to include a utility decrement for bladder instillations

3.13 The company justified modelling a utility decrement for bladder instillations because it considered them to be invasive and associated with adverse effects. The committee noted that the utility decrement was applied for all patients who had bladder instillations for the lifetime of the company's model. It also noted that

the utility score for patients having subsequent bladder instillations was counterintuitive when compared with the utility score for people whose condition did not respond to treatment and who moved onto best supportive care (these results are academic in confidence and cannot be reported here). The ERG noted that the difference in utility score in the survey between people who had and people who had not recently had bladder instillations may have reflected baseline patient characteristics rather than treatment. The clinical experts also added that any decrement associated with bladder instillations was likely to be short-lived because the treatment would be stopped if there were any adverse events. The committee concluded that applying a utility decrement for bladder instillations was not appropriate.

Resource use

It is acceptable to assume 6-weekly administration of subsequent bladder instillations and first-time bladder instillations after the first year

3.14 The company modelled weekly administration of first-time bladder instillations for the first 4 weeks, and 4-weekly administration after this point. This frequency also applied to all subsequent bladder instillations. The clinical experts explained that initial treatment with bladder instillations would be weekly for 4 weeks followed by maintenance treatment once every 4 weeks for 4 to 6 months. Continuation would be based on response to treatment. They also noted that it was reasonable to administer maintenance treatment at 6-weekly intervals for subsequent bladder instillations if this achieved the same response in patients as 4-weekly administration. The patient expert explained that maintenance treatment intervals vary according to the person and can be either monthly or when symptoms return. If maintenance treatment is led by the patient based on their symptoms, this would lengthen the interval between instillations beyond 4 weeks. The ERG's model accounted for this variation. It included 6-weekly maintenance intervals for subsequent bladder instillations and for first-time bladder instillations after a year of treatment. The committee acknowledged the variation in clinical practice and recognised that administration would be different for first-time and subsequent bladder instillations. The committee considered the

company's response to consultation. This outlined that 4-weekly administration is in line with the manufacturer's recommendations, treatment is tailored to individual patient needs, and variability in dosing frequency results in some intervals being shorter than 4-weekly whereas others are longer. However, based on the evidence from the ERG and clinical experts, the committee concluded that it was acceptable to assume 6-weekly administration for subsequent bladder instillations and for first-time bladder instillations after the first year (in line with the ERG's model).

Most people having bladder instillations would not stay on treatment indefinitely

3.15 Both the company's and the ERG's models assumed that bladder instillations were administered indefinitely. The clinical experts explained that bladder instillations would not continue for a lifetime and estimated that only 5% of patients would continue with them after 5 years. The committee acknowledged that in clinical practice bladder instillations would not continue indefinitely and most patients would stop within 5 years. It also recognised that best supportive care becomes a more relevant comparator if more patients stop treatment with bladder instillations.

Inpatient resource use is overestimated in the company's model

3.16 The company's model included a proportion of patients who would have inpatient care for bladder instillations. The ERG noted that the disease-related costs in the company's model had been overestimated because not all of the resource use was a result of bladder pain syndrome with glomerulations or Hunner's lesions. The clinical experts explained that most people having bladder instillations are seen in outpatient care; the number having inpatient care is negligible. The committee considered that the company had overestimated the disease-related costs by modelling a proportion of patients to have inpatient care. The committee concluded that inpatient resource use would be minimal in a population having bladder instillations. However, it was aware that the incremental cost-effectiveness ratio (ICER) was not sensitive to this parameter in the model.

Cost-effectiveness estimates

There are uncertainties in the cost-effectiveness estimates that are unlikely to be resolved

3.17 The committee noted the substantial uncertainty in the model inputs, specifically:

- the considerable variability in the treatment pathway (see section 3.4)
- the significant uncertainty in the pentosan polysulfate sodium evidence (see section 3.7)
- the methodological limitations with all approaches to indirect treatment comparisons (see section 3.8)
- the challenges with the missing data on utility values (see section 3.11).

The committee concluded that these substantial uncertainties were unlikely to be resolved in the cost-effectiveness modelling.

Pentosan polysulfate sodium is likely to be cost effective for bladder pain syndrome compared with bladder instillations

3.18 The company's base case included the following assumptions:

- a lifetime time horizon in the model (issue 2 of the technical report)
- time to discontinuation based on the ERG's time-to-discontinuation data set and a log-normal extrapolation (issue 4 of the technical report)
- a utility decrement associated with having bladder instillations in the previous 6 months (issue 5 of the technical report)
- excluded missing data on previous bladder instillations (issue 5 of the technical report)
- a 4-weekly administration of bladder instillations for first-time and subsequent treatment (issue 7 of the technical report)

- treatment with bladder instillations continued indefinitely (issue 7 of the technical report).

When the confidential commercial arrangement was applied, the company's base-case analysis showed that pentosan polysulfate sodium cost less and had higher quality-adjusted life year (QALY) gain than bladder instillations.

The ERG's analyses included the following committee-preferred assumptions:

- a Bayesian network meta-analysis using the ERG's preferred approach (see section 3.9)
- a lifetime time horizon in the model (issue 2 of the technical report)
- time to discontinuation based on the ERG's time-to-discontinuation data set and a log-normal extrapolation (issue 4 of the technical report)
- treatment with bladder instillations continued indefinitely (see section 3.15)
- no utility decrement associated with having bladder instillations in the previous 6 months (see sections 3.11 to 3.13)
- 6-weekly administration of bladder instillations (see section 3.14).

The ERG's revised ICER using the committee's preferred assumptions and applying the confidential commercial arrangement was £14,418 per QALY gained when compared with bladder instillations. Based on the ERG's analysis, the committee concluded that the most plausible cost-effectiveness estimate for pentosan polysulfate sodium compared with bladder instillations was likely to be a cost-effective use of NHS resources (see NICE's guide to the methods of technology appraisal).

Pentosan polysulfate sodium is unlikely to be cost effective for bladder pain syndrome compared with best supportive care

3.19 The company's base case included the following assumptions:

- a lifetime time horizon in the model (issue 2 of the technical report)

- best supportive care response rates did not recede over time (issue 3 of the technical report)
- 15.8% placebo response rate estimated from the pentosan polysulfate sodium trials (issue 3 of the technical report)
- time to discontinuation based on the ERG's time-to-discontinuation data set and a log-normal extrapolation (issue 4 of the technical report)
- utility scores and costs returned to baseline for people whose condition did not respond to treatment who moved on to best supportive care (issue 6 of the technical report).

The company's base-case ICER compared with best supportive care (including the confidential commercial arrangement) was £52,264 per QALY gained.

The ERG's analyses included the following committee-preferred assumptions:

- a Bayesian network meta-analysis using the ERG's preferred approach (see section 3.9)
- a lifetime time horizon in the model (issue 2 of the technical report)
- best supportive care response rates did not recede over time (issue 3 of the technical report)
- time to discontinuation based on the ERG's time-to-discontinuation data set and a log-normal extrapolation (issue 4 of the technical report)
- utility scores and costs returned to baseline for people whose condition did not respond to treatment who moved on to best supportive care (issue 6 of the technical report)
- 16% placebo response rate from the pentosan polysulfate sodium trials (see section 3.10).

The ERG's revised ICER using the committee's preferred assumptions and applying the confidential commercial arrangement was £50,740 per QALY gained when compared with best supportive care. The committee concluded

that the most plausible cost-effectiveness estimate for pentosan polysulfate sodium compared with best supportive care was higher than usually considered a cost-effective use of NHS resources (see NICE's guide to the methods of technology appraisal).

Positioning of treatment

The complex treatment pathway makes it hard to separate the comparison with bladder instillations from the comparison with best supportive care

3.20 The committee acknowledged that the treatment pathway for bladder pain syndrome was complex and varied between services. The clinical experts advised that pentosan polysulfate sodium would generally be used before bladder instillations or for people who could not have bladder instillations. However, the experts and responses to consultation indicated that pentosan polysulfate sodium may be used after bladder instillations have been tried. The committee accepted that the complex pathway made it difficult to separate populations based on comparators.

Neither the company nor the ERG's models capture the use of pentosan polysulfate sodium in combination with or after bladder instillations

3.21 In the company's and the ERG's models, patients having bladder instillations were assumed to stay on them indefinitely. The models did not capture the cost effectiveness of pentosan polysulfate sodium when it was taken after a lack of response to treatment with bladder instillations. The models also did not capture the cost effectiveness of pentosan polysulfate sodium when it was taken in combination with bladder instillations. The committee concluded that it could not assess the cost effectiveness of pentosan polysulfate sodium for these populations.

Pentosan polysulfate sodium is only for people whose condition has not responded well to other less expensive oral treatments

3.22 The clinical experts stated that there are many different types of oral treatments for bladder pain syndrome and that these have to be tried repeatedly. The committee was aware that best supportive care consisted of less expensive oral treatments than pentosan polysulfate sodium. It was also aware that some people get good disease control from standard oral treatments. The company and clinical experts agreed that pentosan polysulfate sodium would be used after inadequate response to standard oral treatments. The committee concluded that standard oral treatments should be tried first (see section 3.3) and that pentosan polysulfate sodium should only be used for people who have stopped these treatments because of a lack of response.

The proportion of people who have best supportive care because bladder instillations are unsuitable for them is low

3.23 The clinical experts explained that bladder instillations would be unsuitable for less than 5% of people. The committee acknowledged that because this is likely to be a small population, the estimated impact on NHS resources is also likely to be small (see section 6.2.14 in NICE's guide to the methods of technology appraisal).

Conclusion

Pentosan polysulfate sodium is recommended for some people

3.24 The ICER for the comparison with best supportive care was higher than what is considered to be cost effective. But the ICER for the comparison with bladder instillations was considered to be a cost-effective use of NHS resources, taking into account:

- the small proportion of people who would not tolerate bladder instillations or for whom they would not be suitable

- the unmet need for effective treatment options for this population and
- the committee's most plausible assumptions.

Therefore, the committee concluded that pentosan polysulfate sodium is recommended as an option for treating bladder pain syndrome with glomerulations or Hunner's lesions in adults with urinary urgency and frequency and moderate to severe pain, only if:

- their condition has not responded to an adequate trial of standard oral treatments
- it is not offered in combination with bladder instillations
- any previous treatment with bladder instillations was not stopped because of lack of response
- it is used in secondary care and
- the company provides pentosan polysulfate sodium according to the commercial arrangement.

Other factors

There are no equalities issues that can be addressed in the guidance

3.25 The company and a clinical expert highlighted that bladder pain syndrome affects more women than men. However, issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has bladder pain syndrome and the healthcare professional responsible for their care thinks that pentosan polysulfate sodium is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Omar Moreea
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