

# Interstitial cystitis: dimethyl sulfoxide bladder instillation

## Evidence summary

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[nice.org.uk/guidance/esuom26](https://www.nice.org.uk/guidance/esuom26)

## Key points from the evidence

The content of this evidence summary was up-to-date in February 2014. See [summaries of product characteristics](#) (SPCs), [British national formulary](#) (BNF) or the [MHRA](#) or [NICE](#) websites for up-to-date information.

## Summary

This evidence summary is based on 3 small [randomised controlled trials](#) (RCTs). All 3 of the studies were likely to be subject to significant bias and provide limited evidence on the use of dimethyl sulfoxide (DMSO) bladder instillation (Rimso-50) for interstitial cystitis.

**Regulatory status:** unlicensed.

This topic was prioritised because there was a high volume of requests from the NHS for information on this topic and potential for variation in practice.

<p><b>Effectiveness</b></p> <ul style="list-style-type: none"> <li>Assessing the effectiveness of treatments for interstitial cystitis is difficult due to a lack of certainty around the diagnosis and the use of subjective measures of response.</li> <li>More people reported a 'marked improvement' with DMSO compared with placebo (6/15 [40%] compared with 3/17 [18%]; reported as statistically significant; no p value given) [1 RCT; n=33].</li> <li>A Cochrane review included the RCT described above and provided additional statistical analysis not available in the published study. This showed no statistically significant difference between DMSO and placebo for bladder capacity and pain (1 RCT; n=33).</li> <li>Statistically significantly more people reported to be 'much better' or 'completely cured' with DMSO compared with BCG (off-label use) [11/37 (30%) compared with 4/38 (11%); 1 RCT; 3 months; n=75].</li> </ul>	<p><b>Safety</b></p> <ul style="list-style-type: none"> <li>The <a href="#">prescribing information</a> for DMSO (Rimso-50; licensed by the US Food and Drug Administration) states that full eye evaluations including slit lamp examinations are recommended before and periodically during treatment.</li> <li>Biochemical screening, particularly liver and renal function tests, and complete blood count should be done approximately every 6 months.</li> <li>The <a href="#">British national formulary</a> (December 2013) states that bladder spasm and hypersensitivity reactions may occur.</li> </ul>
<p><b>Patient factors</b></p> <ul style="list-style-type: none"> <li>Administration may cause moderately severe discomfort, which may result in the inability to tolerate treatment.</li> <li>May also cause garlic-like taste and odour on the breath and skin that may remain for 72 hours.</li> </ul>	<p><b>Resource implications</b></p> <ul style="list-style-type: none"> <li>DMSO is unlicensed in the UK. No costs could be obtained from standard published sources or the manufacturer<sup>1</sup>.</li> <li>Costs will also be associated with the administration of the bladder instillation.</li> </ul>
<p><sup>1</sup>Informal sources suggest that the cost is around £101 (plus VAT) per 50 ml bladder instillation.</p>	

## Key points

DMSO bladder instillation is unlicensed in the UK. It is available from 'special-order' manufacturers or specialist importing companies.

Three small RCTs were identified for inclusion in this evidence summary. One of the RCTs ([Perez-Marrero et al. 1988](#)) compared DMSO with placebo (saline) and 2 ([Peeker et al. 2000](#) and [Sairanen et al. 2009](#)) compared DMSO with bacillus Calmette-Guerin (BCG) (off-label use). A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) included 1 of these studies ([Perez-Marrero et al. 1988](#)). The Cochrane review also identified the [Peeker et al. \(2000\)](#) study, however the Cochrane review concluded that this study did not provide useful data for any outcome (see [Evidence strengths and limitations](#)).

[Perez-Marrero et al. \(1988\)](#) was a small randomised crossover trial that compared 4 instillations, 2 weeks apart, of DMSO (50 ml of 50% DMSO) with placebo (50 ml of normal saline) in 33 people (30 women; mean age 48 years) with biopsies suggestive of interstitial cystitis. After a 4-week washout period the treatment allocation was reversed and a further 4 instillations given. Assessment followed the completion of each treatment phase and comprised a subjective assessment by participants (rated as minimal [0], moderate or marked) and an objective outcome based on 3 urodynamic parameters. After completion of phase I, 40% (6/15) of people treated with DMSO reported marked subjective improvement in symptoms compared with 18% (3/17) of people receiving placebo. The difference in the proportion of people reporting marked subjective improvement was reported to be statistically significant but no statistical analysis was presented. People in the group that received DMSO at phase I continued to report subjective improvement after treatment with placebo at phase II.

The Cochrane review ([Dawson and Jamison 2007](#)) presented statistical analysis for 2 of the urodynamic parameters which was not available in the published study. This reported that there was no statistical significant difference between DMSO and placebo for maximum cystometric capacity (volume at which a person is unable or unwilling to tolerate continued bladder filling or leakage occurs) [mean difference 17.00 ml; 95% confidence interval [CI] –11.22 to 45.22] or number of people whose pain resolved at maximum cystometric capacity (23/28 compared with 22/28; odds ratio [OR] 0.22; 95% CI –1.10 to 1.55).

[Sairanen et al. \(2009\)](#) was a 3-month randomised open-label trial comparing intravesical instillations of 50 ml 50% DMSO with 50 ml Tice strain BCG (dose of BCG not reported, length of instillation not reported) given once a week for 6 weeks in 75 people (71 women; mean age 59 years) with painful bladder syndrome/interstitial cystitis. The main aim of this study was to

evaluate a health-related quality of life questionnaire in painful bladder syndrome/interstitial cystitis. The primary outcome of the study was alleviation of pain. However, data for this outcome were not reported. Data were reported on subjective global assessment of treatment response. At the 3-month follow-up, more people had a global assessment of treatment response of 'much better' or 'completely cured' with DMSO compared with BCG (11/37 [30%] compared with 4/38 [11%];  $p < 0.05$ ).

All 3 trials were likely to be subject to significant bias. None of them reported the method of randomisation, and whether or not randomisation was concealed was either not reported or unclear. In addition, the studies were either unblinded or blinded but at high risk of unblinding due to the characteristic garlic halitus (breath smelling of garlic) caused by DMSO bladder instillation.

In Perez-Marrero et al. (1988), 3 minor adverse events occurred (2 uncomplicated lower urinary tract infections, 1 case of biliary colic). It is unclear if these occurred during the placebo or DMSO phase. Two severe adverse events occurred during the placebo phase (1 hemiparesis, 1 migraine) but both completely resolved within 48 hours. In Peeker et al. (2000), adverse events reported following DMSO treatment were increased urinary urgency (2 cases) and dysuria (3 cases). Adverse events were not reported in Sairanen et al. (2009).

#### 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.**

## Overview for healthcare professionals

Interstitial cystitis (also known as painful bladder syndrome) is a chronic bladder condition that is 10 times more common in women than men. It is characterised by pain, urinary urgency and frequency, and nocturia. There are cystoscopic and histological features that are said to be typical

of interstitial cystitis. However, in many cases the diagnosis is made by exclusion, once specific causes such as infection and malignancy have been ruled out ([Dawson and Jamison 2007](#)).

Treatments for interstitial cystitis include dietary and lifestyle interventions, oral medication, intravesical instillations and, in some cases, surgery. No single treatment is effective for all subtypes or phenotypes.

### *Regulatory status of dimethyl sulfoxide bladder instillation*

Dimethyl sulfoxide (DMSO) bladder instillation is unlicensed in the UK. A 50 ml solution of 50% DMSO for intravesical instillation ([Rimso-50](#)) is licensed by the [US Food and Drug Administration](#). It is available from '[special-order](#)' manufacturers or [specialist importing companies](#).

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 DMSO.

### *Evidence statements*

- Three small [randomised controlled trials](#) (RCTs) were identified for inclusion in this evidence summary. One of the RCTs ([Perez-Marrero et al. 1988](#)) compared DMSO with placebo and 2 ([Peeker et al. 2000](#) and [Sairanen et al. 2009](#)) compared DMSO with bacillus Calmette-Guerin (BCG) (off-label use). It should be noted that the [European Association of Urology 2012 guidelines on chronic pelvic pain](#) concluded that bladder instillation with BCG is not effective for the treatment of bladder pain syndrome/interstitial cystitis and its use for this indication is not recommended.
- A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) [search date 2006] included 1 of these studies ([Perez-Marrero et al. 1988](#)). The Cochrane review also identified the [Peeker et al. \(2000\)](#) study but concluded that it did not provide useful data for any outcome and did not provide data that contributed to the Cochrane review (see [Evidence strengths and limitations](#)).
- [Perez-Marrero et al. \(1988\)](#) was a small randomised crossover trial that compared DMSO with placebo (saline) in 33 people with biopsies suggestive of interstitial cystitis. More people reported a marked subjective improvement with DMSO than with placebo (6/15 [40%] compared with 3/17 [18%]; reported as statistically significant; no p value given). The Cochrane review ([Dawson and Jamison 2007](#)) presented statistical analysis that was not available in the published study. This reported no statistically significant difference between DMSO and placebo for maximum cystometric capacity (the volume at which a person is unable

or unwilling to tolerate continued bladder filling or leakage occurs) [mean difference 17.00 ml; 95% [confidence interval](#) [CI] –11.22 to 45.22] or the number of people whose pain resolved at maximum cystometric capacity (23/28 compared with 22/28; [odds ratio](#) [OR] 0.22; 95% CI –1.10 to 1.55).

- [Sairanen et al. \(2009\)](#) was a 3-month randomised open-label trial comparing instillations with DMSO to instillations with BCG in 75 people with painful bladder syndrome/interstitial cystitis. The main aim of the study was to evaluate a health-related quality of life questionnaire. At the 3-month follow-up, more people had a global assessment of treatment response of 'much better' or 'completely cured' with DMSO compared with BCG (11/37 [30%] compared with 4/38 [11%];  $p < 0.05$ ).

## *Summary of the evidence*

This section gives a brief summary of the main evidence. A more thorough analysis is given in the [Evidence review](#) section.

### **Efficacy**

This evidence summary is based on 3 small RCTs. One compared DMSO with placebo (saline) ([Perez-Marrero et al. 1988](#)) and 2 ([Peeker et al. 2000](#) and [Sairanen et al. 2009](#)) compared DMSO with BCG (off-label use). A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) [search date 2006] included 1 of these studies [[Perez-Marrero et al. \(1988\)](#)]. The Cochrane review also identified the [Peeker et al. \(2000\)](#) [study](#) but concluded that it did not provide useful data for any outcome and did not provide data that contributed to the Cochrane review (see [Evidence strengths and limitations](#)).

### ***Dimethyl sulfoxide compared with placebo (saline)***

[Perez-Marrero et al. \(1988\)](#) was a crossover trial in 33 people (30 women; mean age 48 years) with biopsies suggestive of interstitial cystitis. People were randomised to receive 4 instillations, 2 weeks apart, of either DMSO (50 ml of 50% DMSO) or placebo (50 ml of normal saline) (phase I). Participants were asked to hold the solution in their bladder for at least 15 minutes. After a 4-week washout period the treatment allocation was reversed and a further 4 instillations given (phase II).

Participants were divided into groups of 15 (DMSO first) and 18 (placebo first) that were statistically comparable in age, severity and duration of symptoms. The method of randomisation and whether randomisation was concealed was not reported. One patient in the placebo first group

was found to be pregnant shortly after the first saline instillation and was removed from the study. Two patients in the placebo-first group dropped out before phase II of the trial.

Assessment followed the completion of each treatment phase and comprised a subjective assessment by participants (participants were asked to rate their treatment response as minimal [0], moderate or marked) and an objective outcome based on 3 urodynamic parameters (see table 1 for description of urodynamic parameters used). Improvement in urodynamic parameters had to be accompanied by improvements in voiding (maximum voided volume or number of nocturia episodes) and/or visual analogue scale (VAS) scores for pain, and urinary urgency and frequency to be considered valid. Participants were blinded to treatment allocation but the garlic halitus (breath smelling of garlic) caused by DMSO bladder instillation makes blinding difficult to maintain. Assessors for the objective outcome were blinded to treatment allocation.

At the completion of phase I, 93% (14/15) of the people treated with DMSO were considered objectively to have experienced improvement compared with 35% (6/17) of the placebo group. No statistical analysis was presented. After crossover, at the completion of phase II, 86% of people initially treated with DMSO at phase I continued to show objective improvement from baseline (13/15). When the placebo group crossed over to DMSO at phase II, 67% of people showed an objective improvement (10/15).

At the completion of phase I, 40% (6/15) of people treated with DMSO and 18% (3/17) of people receiving placebo reported marked subjective improvement in symptoms. The difference in the proportion of people reporting marked subjective improvement was reported to be statistically significant but no statistical analysis was presented. People in the group who received DMSO at phase I continued to report subjective improvement after treatment with placebo at phase II, with 53% (8/15) reporting marked improvement. When the placebo group crossed over to DMSO at phase II, 47% of people (7/15) reported marked improvement.

A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) [search date 2006] included [Perez-Marrero et al. \(1988\)](#) and presented statistical analysis for 2 of the urodynamic parameters that was not available in the published study. The Cochrane review reported that there was no statistically significant difference between DMSO and placebo for maximum cystometric capacity (mean difference 17.00 ml; 95% [confidence interval](#) [CI] -11.22 to 45.22) or the number of people whose pain resolved at maximum cystometric capacity (23/28 compared with 22/28; [odds ratio](#) [OR] 0.22; 95% CI -1.10 to 1.55).

**Table 1 Summary of *Perez-Marrero et al. (1988)***

	Group A	Group B	Analysis
Randomised	n=15	n=18	
Phase I	DMSO	Placebo	
Efficacy	n=15	n=17 <sup>a</sup>	
Objective improvement <sup>b</sup>	93% (14/15)	35% (6/17)	No statistical analysis presented
Subjective marked improvement	40% (6/15)	18% (3/17)	Reported to be statistically different, p value not reported See also Cochrane review: additional statistical analysis <sup>c</sup>
Subjective moderate improvement	47% (7/15)	41% (7/17)	
Phase II	Placebo	DMSO	
Efficacy	n=15	n=15 <sup>d</sup>	
Objective improvement	86% (13/15)	67% (10/15)	
Subjective marked improvement	53% (8/15)	47% (7/15)	
Subjective moderate improvement	33% (5/15)	20% (3/15)	
Cochrane review: additional statistical analysis <sup>c</sup>	DMSO (given as initial or second instillation)	Placebo (given as initial or second instillation)	

Pain resolved at maximum cystometric capacity	23/28	22/28	No statistically significant difference between DMSO and placebo (OR 0.22; 95% CI -1.10 to 1.55)
Maximum cystometric capacity	-	-	No statistically significant difference between DMSO and placebo (mean difference 17 ml; 95% CI -11.22 to 45.22 ml)
Safety			
Patients reporting serious adverse events	2 severe (1 hemiparesis, 1 migraine) both in placebo phase		

Abbreviations: CI, confidence interval; DMSO, dimethyl sulfoxide; n, number of patients; OR, odds ratio.

<sup>a</sup> One patient was found to be pregnant shortly after the first instillation (placebo) and was removed from the study.

<sup>b</sup> Objective improvement was based on 3 urodynamic parameters (improvement by 50% in cystometric urge [the volume at which a person has a strong desire to void but can tolerate continued bladder filling] or maximum cystometric capacity [the volume at which a person is unable or unwilling to tolerate continued bladder filling or leakage occurs] and/or the disappearance of suprapubic pain or urethral pain at maximum cystometric capacity). Improvement in urodynamic parameters had to be accompanied by improvements in voiding (maximum voided volume or number of nocturia episodes) and/or visual analogue scale scores for pain, and urinary urgency and frequency to be considered valid.

<sup>c</sup> A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) includes Perez-Marrero et al. (1988) and presents statistical analysis for 2 of the urodynamic parameters that was not available in the published study.

<sup>d</sup> Two patients dropped out between phase I and phase II.

### ***Dimethyl sulfoxide compared with bacillus Calmette-Guerin***

It should be noted that the [European Association of Urology 2012 guidelines on chronic pelvic pain](#) concluded that bladder instillation with BCG is not effective for the treatment of interstitial

cystitis/bladder pain syndrome and that its use for this indication is not recommended. The use of BCG for interstitial cystitis is off-label.

Peeker et al. (2000) was described as a double-blind crossover RCT. However, it was not a true crossover design because participants only crossed over to the second treatment if they did not improve with the first treatment they were randomised to. Twenty-one participants (20 women) were included, of whom 11 (mean age 59 years) had classic or ulcerative interstitial cystitis and 10 (mean age 43 years) had non-ulcerative interstitial cystitis (based on clinical, endoscopic and histopathological criteria). The trial compared 6 weekly instillations with BCG (retained in the bladder for 2 hours) with 6 weekly instillations of DMSO (50 ml of 50%, duration of retention not reported). Participants not reporting subjective improvement after receiving the first treatment crossed over to the other treatment after a washout period of at least 7 weeks. Analysis of outcomes took place at the end of this washout period.

The primary outcome was subjective improvement (not further defined). The effect of treatment on maximal functional bladder capacity, urinary frequency (both assessed according to patient voiding diaries) and pain (VAS scores) was also reported.

Participants were divided into 2 groups. The number of participants randomised to each group and the number with each type of interstitial cystitis was not given, and the method of randomisation was not reported. It is unclear whether randomisation was concealed. Participants were blinded to treatment allocation but the garlic halitus (breath smelling of garlic) caused by DMSO bladder instillation makes blinding difficult to maintain.

The Cochrane review (Dawson and Jamison 2007) identified this study as part of the systematic review but because insufficient information was provided to allow parallel analysis of the first period of the trial, data from this study did not contribute to the review (see Evidence strengths and limitations).

Two participants who received DMSO as the initial treatment reported improvement and so did not cross over to BCG (no individual data or statistical analysis were presented). None of the participants who received BCG as the initial treatment reported improvement. However, 4 participants in this group withdrew without having crossover treatment despite not improving. Therefore 6 participants received 1 treatment only and 15 participants received both treatments. Apart from these 6 participants it is not possible to confirm group size or order of treatment from the data presented. A further 5 people reported improvement after crossing over to DMSO. The majority of people whose condition responded to treatment were in the group that received BCG first followed by DMSO. It is not clear whether the washout period used in this study was long

enough. It has been reported that a 6-month follow-up after treatment with BCG is needed to define response.

Of the 7 people who reported improvement, 2 remained symptom-free for 12 and 18 months and the remaining 5 relapsed and continued treatment with DMSO. It was not reported whether the participants who showed improvement had ulcerative or non-ulcerative interstitial cystitis.

Sairanen et al. (2009) was a 3-month randomised open-label trial in 75 people (71 women; mean age 59 years) meeting National Institute of Diabetes and Digestive and Kidney Diseases criteria for painful bladder syndrome/interstitial cystitis. It compared intravesical instillations of 50 ml 50% DMSO with 50 ml Tice strain BCG (dose of BCG not reported, length of instillation not reported) given once a week for 6 weeks. The main aim of the study was to evaluate a health-related quality of life (HRQoL) questionnaire in painful bladder syndrome/interstitial cystitis.

Participants were randomised into 2 groups: 37 to DMSO and 38 to BCG. The method of randomisation and whether randomisation was concealed was not reported. The primary outcome of the study was alleviation of pain. However, data for this outcome were not reported. Data were reported on subjective global assessment of treatment response after 3 months, with the condition of participants who scored their response as much better or completely cured considered to have responded to treatment. The HRQoL questionnaire (which included questions relating to general health perceptions, pain, emotional wellbeing, vitality, social functioning, physical capacity and sexual interest and functioning) was also completed before treatment and at the 3-month follow-up.

At the 3-month follow-up, more people had a global assessment of treatment response of 'much better' or 'completely cured' with DMSO compared with BCG (11/37 [30%] compared with 4/38 [11%];  $p < 0.05$ ). After 3 months, if subjective treatment response was not achieved, participants were allowed to cross over to the other treatment group without any specified washout period. A new baseline HRQoL questionnaire and a new outcome questionnaire were obtained at 3 months. DMSO and BCG therapies were reported to have an equal effect on HRQoL ( $p$  value not reported). This analysis combined results after the first instillation therapy with results for participants who had received secondary treatment with DMSO or BCG (without a specified washout period) if their condition had not responded to the initial treatment they were allocated to.

## Safety

### *Adverse events reported in trials*

In [Perez-Marrero et al. \(1988\)](#), adverse events were seen in 5 people (15%). Three were minor (2 uncomplicated lower urinary tract infections, 1 case of biliary colic). It was unclear whether participants were receiving placebo or DMSO at the time of the adverse event. The other 2 adverse events were severe (1 hemiparesis, 1 migraine). Both of these occurred during the placebo phase and resolved completely within 48 hours.

In [Peeker et al. \(2000\)](#) adverse events after DMSO treatment were reported as increased urinary urgency (2 cases) and dysuria (3 cases).

Adverse events were not reported in [Sairanen et al. \(2009\)](#).

### *Other sources of safety information*

Adverse reactions associated with Rimso-50 (50% DMSO instillation licensed by the [US Food and Drug Administration](#)) listed in the [prescribing information](#) are a garlic-like taste and odour on the breath and skin, which may remain for 72 hours, and transient chemical cystitis. Administration may cause moderately severe discomfort. DMSO may cause a hypersensitivity reaction (reported in 1 patient receiving intravesical Rimso-50 solution). Full eye evaluations including slit lamp examinations are recommended before and periodically during treatment. Biochemical screening, particularly liver and renal function tests, and complete blood count should be done approximately every 6 months. Intravesical instillation of Rimso-50 solution may be harmful to people with urinary tract malignancy because of dimethyl-sulfoxide-induced vasodilation.

The [British national formulary](#) (December 2013) states that bladder spasm and hypersensitivity reactions may occur with DMSO and long-term use requires ophthalmic, renal, and hepatic assessment at intervals of 6 months. It also recommends that the concomitant use of DMSO with the non-steroidal anti-inflammatory drug sulindac should be avoided.

The [European Association of Urology 2012 guidelines on chronic pelvic pain](#) state that use of DMSO is contraindicated during urinary tract infections or shortly after bladder biopsy.

## Cost effectiveness and cost

No cost effectiveness studies were identified.

Because DMSO bladder instillation (Rimso-50) is unlicensed in the UK, no costs could be obtained from standard published sources or the manufacturer. It is available from ['special-order' manufacturers or specialist importing companies](#). Informal sources suggest that the cost is around £101 (plus VAT) per 50 ml bladder instillation.

## Relevance to NICE guidance programmes

There is no NICE guidance on interstitial cystitis or painful bladder syndrome.

This use of dimethyl sulfoxide (DMSO) is not appropriate for referral for a NICE technology appraisal and is not currently planned into any other work programme.

## Intervention and alternatives

DMSO bladder instillation is unlicensed in the UK, but a 50% DMSO solution for intravesical instillation ([Rimso-50](#)) is licensed by the [US Food and Drug Administration](#). It is available from ['special-order' manufacturers or specialist importing companies](#).

## Condition

Interstitial cystitis (also known as painful bladder syndrome) is a chronic bladder condition that is 10 times more common in women than men. It is characterised by pain, urinary urgency and frequency, and nocturia. There are cystoscopic and histological features that are said to be typical of interstitial cystitis. However, in many cases the diagnosis is made by exclusion, once specific causes such as infection and malignancy have been ruled out ([Dawson and Jamison 2007](#)).

The [European Association of Urology 2012 guidelines on chronic pelvic pain](#) describes interstitial cystitis as a chronic distressing bladder condition. It states that interstitial cystitis has been shown to encompass a heterogeneous spectrum of disorders, with different endoscopic and histopathological presentations, with inflammation an important feature in only a subset of patients. To embrace all patients suffering from bladder pain, the terms painful bladder syndrome or bladder pain syndrome have been suggested as more accurate when referring to pain in the bladder region, while assuming interstitial cystitis with Hunner's lesion as a specific type of chronic inflammation of the bladder. The guidelines recommend that bladder pain syndrome should be diagnosed on the basis of pain, pressure or discomfort associated with the urinary bladder, accompanied by at least one other symptom such as daytime and/or night-time increased urinary frequency, the exclusion of confusable diseases as the cause of symptoms, and if indicated cystoscopy with hydrodistension and biopsy. It can then be subtyped according to the results of

cystoscopy with hydrodistension and biopsy. It can also be further classified according to phenotype which classifies the condition according to the person's clinical symptoms.

## *Alternative treatment options*

European Association of Urology 2012 guidelines on chronic pelvic pain recommend that therapy for interstitial cystitis (or their term, bladder pain syndrome [BPS]) is subtype and phenotype orientated, and that multimodal behavioural, physical and psychological techniques should always be considered alongside oral or invasive treatments. No single treatment is effective for all subtypes or phenotypes. A variety of potential treatment options including intravesical DMSO are recommended in the guidelines.

Treatment regimens often have to be flexible to cover a variety of symptoms that change over time.

A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis (Dawson and Jamison 2007) [search date 2006] concluded that the evidence base for treating painful bladder syndrome/interstitial cystitis using intravesical preparations is limited.

## **Evidence review: efficacy**

This evidence summary is based on 3 small randomised controlled trials (RCTs). One compared DMSO with placebo (saline) (Perez-Marrero et al. 1988) and 2 (Peeker et al. 2000 and Sairanen et al. 2009) compared DMSO with bacillus Calmette-Guerin (BCG) (off-label use). A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis (Dawson and Jamison 2007) [search date 2006] included 1 of these studies (Perez-Marrero et al. 1988). The Cochrane review also identified the Peeker et al. (2000) study but concluded that it did not provide useful data for any outcome and did not provide data that contributed to the Cochrane review (see Evidence strengths and limitations).

### *DMSO compared with placebo (saline)*

Perez-Marrero et al. (1988) was a crossover trial in 33 people (30 women and 3 men; mean age 48 years) with biopsies suggestive of interstitial cystitis. The participants were described as being in the 'early stages' of the disease and none of them had contracted bladders or Hunner's ulcers. The mean duration of symptoms was 5.5 years. The presentation of symptoms was varied (16 people had pain as a significant component of the symptom complex, 28 had urinary urgency and frequency, and 22 had nocturia). People were randomised to receive 4 instillations, 2 weeks apart, of either DMSO (50 ml of 50% DMSO) or placebo (50 ml of normal saline) (phase I). Participants

were asked to hold the solution in their bladder for at least 15 minutes. After a 4-week washout period the treatment allocation was reversed and a further 4 instillations given (phase II).

Assessment followed the completion of each treatment phase and comprised a subjective assessment by participants (participants were asked to rate their treatment response as minimal [0], moderate or marked) and an objective outcome based on 3 urodynamic parameters (improvement by 50% in cystometric urge [the volume at which a person has a strong desire to void but can tolerate continued bladder filling] or maximum cystometric capacity [the volume at which a person is unable or unwilling to tolerate continued bladder filling or leakage occurs] and/or the disappearance of suprapubic pain or urethral pain at maximum cystometric capacity). Improvement in urodynamic parameters had to be accompanied by improvements in voiding (maximum voided volume or number of nocturia episodes) and/or visual analogue scale (VAS) scores for pain, and urinary urgency and frequency to be considered valid. Participants were blinded to treatment allocation but the garlic halitus (breath smelling of garlic) caused by DMSO bladder instillations makes blinding difficult to maintain. Assessors for the objective outcome were blinded to treatment allocation.

Participants were divided into groups of 15 (DMSO first) and 18 (placebo first) that were statistically comparable in age, severity and duration of symptoms. The method of randomisation and whether randomisation was concealed was not reported. One patient in the placebo-first group was found to be pregnant shortly after the first saline instillation and was removed from the study.

At the completion of phase I, 93% (14/15) of people treated with DMSO were considered to have objectively improved compared with 35% (6/17) of the placebo group. No statistical analysis was presented.

At the completion of phase I, 40% (6/15) of people treated with DMSO reported marked subjective improvement in symptoms and 47% (7/15) reported moderate improvement in symptoms, whereas 18% (3/17) of people receiving placebo reported marked improvement and 41% (7/17) reported moderate improvement. The difference in the proportion of people reporting marked subjective improvement in symptoms was reported to be statistically significant but no statistical analysis was presented.

Two people in the placebo-first group dropped out before phase II of the trial. After crossover, at the completion of phase II, 86% of people initially treated with DMSO at phase I continued to show objective improvement from baseline (13/15). When the placebo group crossed over to DMSO at phase II, 67% of people showed an objective improvement (10/15).

People in the group who receiving DMSO at phase I continued to report subjective improvement after treatment with placebo at phase II, with 53% (8/15) reporting marked improvement and 33% (5/15) moderate improvement, while 47% (7/15) of people treated with DMSO in phase II reported marked improvement and 20% (3/15) reported moderate improvement. The differences in the numbers of people reporting marked subjective improvement was reported to be statistically significant, however no statistical analysis was presented.

A Cochrane review on intravesical treatments for painful bladder syndrome/interstitial cystitis ([Dawson and Jamison 2007](#)) [search date 2006] included [Perez-Marrero et al. \(1988\)](#) and presented statistical analysis for 2 of the urodynamic parameters that was not available in the published study. The Cochrane review reported that there was no statistically significant difference between DMSO and placebo for maximum cystometric capacity (mean difference 17.00 ml; 95% confidence interval [CI] – 11.22 to 45.22) or the number of people whose pain resolved at maximum cystometric capacity (23/28 compared with 22/28; odds ratio [OR] 0.22; 95% CI – 1.10 to 1.55).

### *DMSO compared with bacillus Calmette-Guerin*

It should be noted that the [European Association of Urology 2012 guidelines on chronic pelvic pain](#) concluded that bladder instillation with bacillus Calmette-Guerin (BCG) is not effective for the treatment of interstitial cystitis/bladder pain syndrome and that its use for this indication is not recommended. The use of BCG for interstitial cystitis is off-label.

[Peeker et al. \(2000\)](#) was described as a double-blind crossover RCT. However it was not a true crossover design in that participants only crossed over to the second treatment if they did not improve with the first treatment they were randomised to. Twenty-one participants (20 women) who met [National Institute of Diabetes and Digestive and Kidney Diseases \(NIDDK\)](#) criteria for interstitial cystitis, of which 11 (mean age 59 years) had classic or ulcerative interstitial cystitis and 10 (mean age 43 years) had non-ulcerative interstitial cystitis (based on clinical, endoscopic and histopathological criteria) were included. Participants were randomised to 6 weekly instillations via catheter with BCG ( $5 \times 10^8$  colony forming units, reconstituted with 1 ml of saline and diluted with 50 ml saline, retained in the bladder for 2 hours) or 6 weekly instillations of DMSO (50 ml of 500 mg/ml, duration of retention not reported). If people did not report subjective improvement they crossed over to the other treatment after a washout period of at least 7 weeks. Analysis of outcomes took place at the end of this washout period. The primary outcome was subjective improvement (not further defined). The effect of treatment on maximal functional bladder capacity, urinary frequency (both assessed according to patient voiding diaries) and pain (VAS scores) was also reported.

Participants were divided into 2 groups. The number of participants randomised to each group and the number with each type of interstitial cystitis was not given, and the method of randomisation was not reported. It is unclear if randomisation was concealed. Participants were blinded to treatment allocation but the garlic halitus (breath smelling of garlic) caused by DMSO bladder instillation makes blinding difficult to maintain.

The Cochrane review ([Dawson and Jamison 2007](#)) identified this study as part of the systematic review but because there was insufficient information provided to allow parallel analysis of the first period of the trial, data from this study were not included in the review (see [Evidence strengths and limitations](#)).

Two participants who received DMSO as the initial treatment reported improvement and so did not cross over to BCG (no individual data or statistical analysis was presented). None of the participants who received BCG as the initial treatment reported improvement. However, 4 participants in this group withdrew without having crossover treatment despite not improving. Therefore 6 participants received 1 treatment only and 15 participants received both treatments. Apart from these 6 participants it is not possible to confirm group size or order of treatment from the data presented. A further 5 people reported improvement after crossing over to DMSO. The majority of people whose condition responded to treatment were in the group that received BCG first followed by DMSO. It is not clear whether the washout period used in this study was long enough. It has been [reported](#) that a 6-month follow-up after treatment with BCG is needed to define response.

Of the 7 people who reported improvement, 2 remained symptom-free for 12 and 18 months and the remaining 5 relapsed and continued treatment with DMSO. It was not reported whether the participants who showed improvement had ulcerative or non-ulcerative interstitial cystitis.

Results were also given for the 3 outcomes of maximal functional bladder capacity, urinary frequency (voids per 24 hours) and pain (VAS score) following either treatment and compared with baseline. Results were reported according to whether participants had ulcerative or non-ulcerative interstitial cystitis.

In participants with ulcerative interstitial cystitis, average maximal functional capacity at baseline was 200 ml (range 100–350 ml). After treatment with BCG, maximal functional capacity was 174 ml (range 60–300 ml) and after DMSO treatment it was 250 ml (190–400 ml). Urinary frequency at baseline was 18 (range 12–28). After DMSO treatment, urinary frequency was reduced to 13 (range 8–16); this was reported to be statistically significant ( $p < 0.05$ ). After BCG treatment, urinary frequency was 17 (range 11–22). Pain (VAS score) at baseline was 6 (range

2–10). After DMSO treatment this was reduced to 2 (range 1–4); this was reported to be statistically significant ( $p < 0.05$ ). After BCG treatment, VAS score was 6 (range 1–10).

In people with non-ulcerative interstitial cystitis, average maximal functional capacity at baseline was 298 ml (range 200–500 ml). After treatment with BCG, maximal functional capacity was 343 ml (range 240–550 ml) and after DMSO treatment it was 344 ml (200–650 ml). Urinary frequency at baseline was 15 (range 8–39). After treatment with BCG, urinary frequency was 11 (range 8–17) and after DMSO treatment it was 11 (8–17). Pain (VAS score) at baseline was 6 (range 1–8). After DMSO treatment this was reduced to 4 (range 1–7); this was reported to be statistically significant ( $p < 0.05$ ). After BCG treatment, VAS score was 5 (range 1–9).

Sairanen et al. (2009) was a 3-month randomised open-label trial in 75 people meeting NIDDK criteria for painful bladder syndrome/interstitial cystitis. The main aim of the study was to evaluate a health-related quality of life (HRQoL) questionnaire in painful bladder syndrome/interstitial cystitis. Participants were randomised to intravesical instillations with 50 ml of 50% DMSO or 50 ml Tice strain BCG (dose of BCG not reported, length of instillation not reported) given once a week for 6 weeks. The primary outcome of the study was alleviation of pain (VAS score). However, data for this outcome were not reported. Thirty-seven people were randomised to DMSO and 38 to BCG. The method of randomisation and whether randomisation was concealed was not reported. Participants randomised to DMSO were all women and at baseline were aged  $61.4 \pm 11.3$  years, had symptoms for  $11.3 \pm 10.1$  years, had urinary frequency per 24 hours of  $14.2 \pm 5.7$ , had  $4.0 \pm 2.5$  nocturia episodes, had a mean voided volume of  $147 \pm 58$  ml and mean pain scores of  $6.4 \pm 2.1$  (VAS score). Of the participants randomised to BCG, 34 were female and 4 were male. At baseline they had a mean age of  $57.9 \pm 14.7$  years, had symptoms for  $8.5 \pm 8.5$  years, had urinary frequency per 24 hours of  $14.2 \pm 6.1$ , had  $4.1 \pm 2.6$  nocturia episodes, had a mean voided volume of  $140 \pm 63$  ml and pain score of  $6.8 \pm 2.1$  (VAS score).

The HRQoL questionnaire (which included questions relating to general health perceptions, pain, emotional wellbeing, vitality, social functioning, physical capacity and sexual interest and functioning) was completed before treatment and also at 3-month follow-up. Data were reported on subjective global assessment of treatment response after 3 months (1=worse, 2=no change, 3=slightly better, 4=moderately better, 5=much better, 6=completely cured), with the condition of participants who scored their response as 5 or 6 considered to have responded to treatment.

At 3 months, if subjective treatment response was not achieved, people were allowed to cross over to the other treatment group without any specified washout period. A new baseline HRQoL questionnaire and a new outcome questionnaire at 3 months were obtained. After the initial 3-month trial, 13 people in the BCG group crossed over to DMSO and 12 people in the DMSO

group changed to BCG. It was reported that 6 people in the DMSO group and 7 in the BCG group dropped out before the 3-month final evaluation. It was not clear whether these people dropped out during the initial 3-month trial or after crossing-over to the alternative treatment.

When only the first initial instillation therapy was considered, more people responded to DMSO than BCG (global assessment of treatment response score 5 or 6; 11/37 [30%] compared with 4/38 [11%];  $p < 0.05$ ).

DMSO and BCG therapies were reported to have an equal effect on HRQoL (p value not reported). This analysis combined results after the first instillation therapy with results for participants who had received secondary treatment with DMSO or BCG (without a specified washout period) if there was no treatment response to the initial treatment they were allocated to.

## Evidence review: safety

### *Adverse events reported in trials*

In [Perez-Marrero et al. \(1988\)](#), 2 participants withdrew from the placebo group before crossing over to DMSO. Adverse events were seen in 5 people (15%). Three were minor and did not need interruption of therapy (2 uncomplicated lower urinary tract infections, 1 case of biliary colic). It was unclear whether participants were receiving placebo or DMSO at the time of the adverse event. The other 2 were severe (1 hemiparesis, 1 migraine) but completely resolved within 48 hours. Both of these occurred during the placebo phase.

In [Peeker et al. \(2000\)](#) adverse events following DMSO treatment were reported as increased urinary urgency (2 cases) and dysuria (3 cases).

In [Sairanen et al. \(2009\)](#) it was reported that 6 people in the DMSO group and 7 in the BCG group dropped out before the 3-month final evaluation. It was not clear whether these people dropped out during the initial 3-month trial or after crossing over to the alternative treatment. No adverse events were reported.

### *Other sources of safety information*

Adverse reactions associated with Rimso-50 (50% DMSO instillation licensed by the [US Food and Drug Administration](#)) listed in the [prescribing information](#) are a garlic-like taste and odour on the breath and skin, which may remain for 72 hours, and transient chemical cystitis. Administration may cause moderately severe discomfort. DMSO may cause a hypersensitivity reaction (reported

in 1 patient receiving intravesical Rimso-50 solution). Full eye evaluations including slit lamp examinations are recommended before and periodically during treatment. Biochemical screening, particularly liver and renal function tests, and complete blood count should be done approximately every 6 months. Intravesical instillation of Rimso-50 solution may be harmful to people with urinary tract malignancy because of dimethyl-sulfoxide-induced vasodilation.

The [British national formulary](#) (December 2013) states that bladder spasm and hypersensitivity reactions may occur and long-term use requires ophthalmic, renal, and hepatic assessment at intervals of 6 months. It also recommends that the concomitant use of DMSO with the non-steroidal anti-inflammatory drug sulindac should be avoided.

The [European Association of Urology 2012 guidelines on chronic pelvic pain](#) state that use of DMSO is contraindicated during urinary tract infections or shortly after bladder biopsy. It also states that there is a case report in which DMSO treatment may have caused pigmented eye lens deposits, therefore ophthalmic review should be considered during treatment.

The [British Association of Urological Surgeons procedure-specific information for patients](#) lists common adverse events (affecting more than 1 person in 10) associated with intravesical instillation of DMSO as: pain/discomfort during treatment resulting in inability to tolerate the treatment for the full period; discolouration of urine; blood in urine; and garlic-like smell in urine and on clothes. Occasional adverse events (affecting between 1 in 10 and 1 in 50 people) are urine infection and failure to relieve symptoms completely requiring further treatment. A rare event (affecting fewer than 1 in 50 people) is inability to pass urine (retention of urine). Hospital-acquired infections are very rare events (colonisation with methicillin-resistant *Staphylococcus aureus* [MRSA] 0.9%; *Clostridium difficile* bowel infection 0.01%; MRSA bloodstream infection 0.02%). The rates of hospital-acquired infection may be greater in high-risk patients (for example, people with long-term drainage tubes, those who have had their bladder removed because of cancer or people who have had previous infections, prolonged hospitalisation or multiple hospital admissions).

## Evidence review: economic issues

### Cost

No cost effectiveness studies were identified.

Because dimethyl sulfoxide (DMSO) bladder instillation (Rimso-50) is unlicensed in the UK, no costs could be obtained from standard published sources or the manufacturer. It is available from

'special-order' manufacturers or specialist importing companies. Informal sources suggest that the cost is around £101 (plus VAT) per 50 ml bladder instillation.

## *Current drug usage*

The Medicines and Healthcare Products Regulatory Agency prepares a summary report of the importation of unlicensed medicines detailing the top 50 products by rank order of number of notifications of import received (by calendar quarter). In the second quarter of 2007, 42 notifications for DMSO (Rimso-50) were received. Since 2007, DMSO has not been included in the list of top 50 products imported.

## **Evidence strengths and limitations**

Only 3 small randomised controlled trials (RCTs) were identified that assessed dimethyl sulfoxide (DMSO) bladder instillation for interstitial cystitis. None of the trials included long-term follow-up. All 3 trials were likely to be subject to significant bias.

Perez-Marrero et al. (1988) compared instillation with DMSO with instillation with saline (placebo) in a small randomised crossover trial in 33 people with biopsies suggestive of interstitial cystitis. The method of randomisation and whether randomisation was concealed was not reported. However, the groups were comparable at baseline.

Participants were blinded to treatment allocation but the garlic halitus (breath smelling of garlic) caused by DMSO bladder instillations makes blinding difficult to maintain. The group randomised to DMSO in the first phase maintained its numbers throughout the study. One patient in group B was found to be pregnant shortly after first instillation of placebo and was removed from the study. Two participants dropped out after placebo before crossing over to DMSO.

Outcomes were assessed using both subjective and objective criteria, and results were reported for both phases of the study. Assessors for the objective response were blinded to treatment allocation.

Peeker et al. (2000) and Sairanen et al. (2009) compared instillation with DMSO with instillation with bacillus Calmette-Guerin (BCG) (off-label use). It should be noted that the European Association of Urology 2012 guidelines on chronic pelvic pain concluded that bladder instillation with BCG is not effective for bladder pain syndrome and that its use for this indication is not recommended.

Peeker et al. (2000) compared instillation with DMSO with instillation with BCG in a small double-blind crossover RCT. The number of participants randomised to each group and the method of randomisation were not reported. It is unclear if randomisation was concealed.

A Cochrane review on intravesical treatments for interstitial cystitis (Dawson and Jamison 2007) identified the Peeker et al. (2000) study but the results from this study did not contribute to the review. This was because of the poor quality of data in the study. The study did not specify the number of participants in either group during the initial instillation and treatment crossover only occurred if the first treatment was ineffective.

Participants were blinded to treatment allocation but as in Perez-Marrero et al. (1988) garlic halitus (breath smelling of garlic) caused by DMSO bladder instillation makes blinding difficult to maintain. The length of time DMSO instillations were held in the bladder was not reported, but the BCG was held for 2 hours. In Perez-Marrero et al. (1988) DMSO was held for 15 minutes. If this was the case, the difference in the length of time the instillations were held for could have led to unblinding.

Four participants who were randomised to BCG for the initial treatment dropped out before crossover to DMSO. No participants who were randomised to DMSO dropped out, but the condition of 2 patients responded to treatment and they did not cross over. The primary outcome was subjective improvement. This was not defined.

The effect of treatment on maximal functional capacity, urinary frequency (both assessed according to patient voiding diaries) and pain (VAS scores) was also reported, according to whether participants had ulcerative or non-ulcerative interstitial cystitis. Data after the first treatment only were not presented. The number of participants in each subgroup, and whether they received BCG or DMSO as the initial treatment, was not reported. It is not clear whether the washout period (at least 7 weeks) used in this study was long enough because it has been reported that a 6-month follow-up after treatment with BCG is needed to define response.

Sairanen et al. (2009) compared instillation with DMSO with instillation with BCG in a randomised open-label trial in 75 people meeting National Institute of Diabetes and Digestive and Kidney Diseases criteria for painful bladder syndrome/interstitial cystitis. The main aim of this study was to evaluate a health-related quality of life questionnaire in painful bladder syndrome/interstitial cystitis.

The dose of BCG administered was not reported, nor was the length of time the instillations were held for. The method of randomisation and whether randomisation was concealed was not

reported. The authors reported that the groups were comparable at baseline, however patients in the BCG group had not been symptomatic on average for as long as those in the DMSO group.

This was an open-label trial, so participants were aware of whether they were receiving instillations with DMSO or BCG. Six patients in the DMSO group and 7 patients in the BCG dropped out of the study; the reasons for doing so were not reported.

The primary outcome of the study was alleviation of pain. However, data for this outcome were not reported. Data were reported on subjective global assessment of treatment response after 3 months. Health-related quality of life data were also reported, but outcomes from the end of the 3-month trial could not be extracted. At the end of the 3-month trial, participants were allowed to switch treatments if they wished to, without a specified washout period. Health-related quality of life data were combined for first and second treatments.

## Summary for patients

A [summary written for patients](#) is available on the NICE website.

## References

British national formulary (2013) [Bladder instillations and urological surgery](#) [online; accessed 13 December 2013]

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US Food and Drug Administration (2013) [Homepage](#) [online; accessed 22 November 2013]

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Peeker R, Haghsheno MA, Holmang S et al. (2000) Intravesical bacillus Calmette-Guerin and dimethyl sulfoxide for treatment of classic and nonulcer interstitial cystitis: a prospective, randomized double-blind study. *Journal of Urology* 164: 1912–5

Perez-Marrero R, Emerson LE, Feltis JT (1988) A controlled study of dimethyl sulfoxide in interstitial cystitis. *Journal of Urology* 140: 36–9

Sairanen J, Leppilahti M, Tammela TL et al. (2009) Evaluation of health-related quality of life in patients with painful bladder syndrome/interstitial cystitis and the impact of four treatments on it. *Scandinavian Journal of Urology* 43: 212–9

The British Association of Urological Surgeons (2012) Intravesical DMSO for painful bladder conditions. [online; accessed 22 November 2013]

## Development of this evidence summary

This evidence summary was developed for NICE by Bazian Ltd. 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.

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## *Declarations of interest*

No relevant interests declared.

## **Appendix: Search strategy and evidence selection**

### *Search strategy*

General background, guidelines and technology assessments:

- Broad internet search: [Google](#), for example: allintext: interstitial OR cystitis "dimethyl sulfoxide" filetype:pdf
- [Trip Database](#)

### **MEDLINE (via Ovid)**

1 Cystitis, Interstitial/ (1502)

2 (interstitial adj3 cystitis).tw. (2366)

3 (pain\$ adj3 bladder).tw. (1194)

4 (inflammatory adj3 bladder).tw. (221)

5 or/1-4 (3245)

6 Dimethyl Sulfoxide/ (13361)

7 (dimethyl sulfoxide or dimethylsulfoxide or DMSO or sulfoxide dimethyl or dimethyl sulphoxide or rimso\$ or sulfnylbis or sclerosol or rheumabene).tw. (21629)

8 or/6-7 (26559)

9 5 and 8 (129)

10 limit 9 to english language (111)

## Embase (via Ovid)

1 Cystitis, Interstitial/ (3034)

2 (interstitial adj3 cystitis).tw. (2794)

3 (pain\$ adj3 bladder).tw. (1716)

4 (inflammatory adj3 bladder).tw. (253)

5 or/1-4 (4494)

6 Dimethyl Sulfoxide/ (17329)

7 (dimethyl sulfoxide or dimethylsulfoxide or DMSO or sulfoxide dimethyl or dimethyl sulphoxide or rimso\$ or sulfnylbis or sclerosol or rheumabene).tw. (20754)

8 or/6-7 (26068)

9 5 and 8 (306)

10 limit 9 to english language (274)

11 limit 10 to exclude medline journals (19)

## Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Cystitis, Interstitial] explode all trees 70

#2 "interstitial cystitis":ti,ab,kw (Word variations have been searched) 112

#3 pain\* near/3 bladder:ti,ab,kw (Word variations have been searched) 69

#4 inflammatory near/3 bladder:ti,ab,kw (Word variations have been searched) 1

#5 #1 or #2 or #3 or #4 154

#6 MeSH descriptor: [Dimethyl Sulfoxide] explode all trees 116

#7 "dimethyl sulfoxide":ti,ab,kw (Word variations have been searched) 159

#8 (rimso\* or DMSO or dimethyl sulphoxide):ti,ab,kw (Word variations have been searched) 121

#9 #6 or #7 or #8 191

#10 #5 and #9 8

[Limit to Trials] 7

## CRD HTA, DARE and EED database

#1 MeSH descriptor: [Cystitis, Interstitial] explode all trees 70

#2 "interstitial cystitis":ti,ab,kw (Word variations have been searched) 112

#3 pain\* near/3 bladder:ti,ab,kw (Word variations have been searched) 69

#4 inflammatory near/3 bladder:ti,ab,kw (Word variations have been searched) 1

#5 #1 or #2 or #3 or #4 154

#6 MeSH descriptor: [Dimethyl Sulfoxide] explode all trees 116

#7 "dimethyl sulfoxide":ti,ab,kw (Word variations have been searched) 159

#8 (rimso\* or DMSO or dimethyl sulphoxide):ti,ab,kw (Word variations have been searched) 121

#9 #6 or #7 or #8 191

#10 #5 and #9 in Other Reviews, Technology Assessments and Economic Evaluations 0

## Grey literature and ongoing trials

- [NHS Evidence](#)
- [Health Canada – Clinical Trials Search](#)
- [ClinicalTrials.gov](#)

## Manufacturer's website

[Bioniche Pharma](#)

## *Evidence selection*

This evidence summary has included randomised controlled trials that have investigated the efficacy of dimethyl sulfoxide bladder instillation for the treatment of interstitial cystitis.

## About 'Evidence summaries: unlicensed or off-label medicines'

NICE evidence summaries for off-label or unlicensed 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. They 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.

This document provides a summary of the published evidence. The strengths and weaknesses of the identified evidence are critically reviewed within this summary, but this summary is not NICE guidance and does not provide formal practice recommendations.

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