



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1466 – Vertebroplasty for severely painful osteoporotic vertebral fractures of less than 6 weeks duration

Applicant: The Interventional Radiology Society of Australasia (IRSA)

Date of MSAC consideration: MSAC 75th Meeting, 28-29 March 2019
MSAC 74th Meeting, 22-23 November 2018

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application

A resubmission requesting Medicare Benefit Schedule (MBS) relisting for vertebroplasty for the treatment of osteoporotic vertebral fractures was received from the Interventional Radiology Society of Australasia (IRSA) by the Department of Health.

2. MSAC's advice to the Minister – March 2019 consideration

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC deferred its advice regarding public funding of vertebroplasty for severely painful osteoporotic vertebral fractures of less than either 3 or 6 weeks duration. MSAC considered that a stakeholder meeting, to provide a broader clinical perspective and patient input, could inform the uncertainties in the application.

MSAC also considered that an independent meta-analysis of the individual patient data (IPD) from all relevant randomised trials would be informative to further address uncertainties, particularly to clarify any consequences of the identified clinical heterogeneity across these trials on the observed effects of vertebroplasty.

MSAC advised that this further information would need to be considered via ESC.

Summary of consideration and rationale for MSAC's advice – March 2019

Vertebroplasty was previously listed on the MBS as an interim-funded service (items 35400 and 35402) from 2005 to 2011. MSAC reviewed this service in April 2011 and did not support continued public funding based on two randomised controlled trials (RCTs) that did not appear to support vertebroplasty. Application 1466 was submitted after publication of a new RCT (VAPOUR) in 2016. The VAPOUR trial was a blinded sham-controlled trial conducted in Australia, with a member of IRSA (the applicant) being the chief investigator.

MSAC considered the application in November 2018, but did not support MBS funding at that time. MSAC acknowledged that there may be a small clinical benefit, but was uncertain of its magnitude or clinical significance. Without a reliable estimate of effect, MSAC considered that cost-effectiveness was highly uncertain, with substantial risk of use beyond the proposed patient population.

At the hearing, representatives of the applicant reiterated that vertebroplasty is intended for use in a specific patient group, primarily elderly female patients who were previously functioning well with sudden onset of immobilisation due to severe pain resulting from a vertebral fracture after a minor injury or fall. These patients present to their general practitioner or emergency department and are admitted for pain relief, usually opiates (with associated side effects including confusion and delirium which further reduces attempts at mobilisation). Representatives of the applicant stated that vertebroplasty is the only alternative to opiates for managing pain in these patients, and leads to more rapid mobilisation.

MSAC noted there is some uncertainty about the harms of the procedure; none of the trials were powered to look at potential harms. MSAC considered that there are potential risks associated with both the procedure itself and the frailty of the patient group. MSAC noted that, in the vertebroplasty group of the VAPOUR trial, there were two serious adverse events related to the procedure (one related to sedation, the other to a fracture during transfer for radiology). The two most severe adverse events were in the control group due to spinal cord compression and retropulsion related to the fracture, one of which led to paraplegia. MSAC considered that it would be valuable to have more details about the patient who became paraplegic – for example, what imaging showed and whether they had any neurological symptoms. At the hearing, the representatives of the applicant confirmed that there was a data safety committee that monitored adverse events in hospitalised patients in the VAPOUR trial. The representatives of the applicant stated that complications were rare in their practice; they knew of only one major severe adverse outcome after the procedure (which was done outside the VAPOUR trial by an inexperienced operator).

MSAC raised concerns about whether vertebroplasty is associated with new fractures near the original site or whether patients who have had vertebroplasty are likely to require repeat treatment. At the hearing, the representatives of the applicant stated that repeat procedures have been done, months apart, in some patients who request vertebroplasty because it was effective for them the first time. The representatives of the applicant stated that pooled data from RCTs shows no difference in the incidence of new fractures due to vertebroplasty in an adjacent vertebrae. However, the representatives of the applicant also stated that patients with osteoporosis (in which previous fractures become hardened, which mimics vertebroplasty) have four times the risk of new fractures. Osteoporosis must therefore be actively treated after vertebroplasty. The representatives of the applicant stated that 40% of patients in the VAPOUR trial were already being treated for osteoporosis, but remained at high risk of fracture. MSAC considered that post-procedure management of osteoporosis also needs to be considered, especially use of denosumab (PBS-listed for this indication).

MSAC considered that there is moderate certainty of a small effect attributable to vertebroplasty, but there is still some uncertainty about the magnitude and clinical importance of that effect.

MSAC recalled that VAPOUR trial participants had one or two osteoporotic fractures of <6 weeks duration and a baseline numeric rating scale (NRS) pain score of $\geq 7/10$. MSAC noted that the primary outcome of the VAPOUR trial was a reduction in NRS pain score to

≤4/10 at 14 days. Secondary outcomes included mean reductions in NRS and visual analogue scale (VAS) pain scores and Roland-Morris disability questionnaire (RDQ) score, quality of life improvements (measured by QUALEFFO and EQ-5D questionnaires), and analgesic use. MSAC noted the VAPOUR trial showed statistically significant reductions in pain scores, modest effects in RDQ scores and variable effects for other outcomes, and effects seemed to somewhat time dependent.

MSAC recalled that the original application proposed a fracture duration of ≤6 weeks as a patient eligibility criterion. After feedback from the Contracted Assessment and Critique, the applicant proposed a fracture duration of ≤3 weeks for consideration at the November 2018 MSAC meeting, consistent with about 80% of patients in the VAPOUR trial. MSAC noted additional analyses of pain results limited to the subgroup of VAPOUR trial patients (n = 95) with fractures ≤3 weeks old provided by the applicant for the current reconsideration. MSAC noted that, in this subgroup, and consistent with the overall intention-to-treat population, significantly more patients in the vertebroplasty arm achieved an NRS pain score of ≤4/10 after 14 days than in the sham arm, and the difference between the groups was maintained out to at least 6 months. The representatives of the applicant noted that these results were confirmed in an independent open-label randomised trial by Yang et al (n = 135), which was also limited to a fracture duration of ≤3 weeks.

MSAC noted results of a post-hoc subgroup analysis of patients in the VAPOUR trial assessing the treatment effect modification of varying the age of the fracture (≤3 weeks vs >3 weeks) against the treatment effect of the primary end point (NRS pain score <4/10 at 14 days) showed that the *P* value for interaction was non-significant (*P* = 0.12). Based on this (and other clinical data), MSAC considered that there is very low certainty that age of fracture (up to 9 weeks) is a treatment effect modifier. MSAC instead noted that the VAPOUR trial post-hoc analysis appeared to show a stronger signal (*P* = 0.0012) for treatment effect modification based on the fracture site, with no apparent benefit for non-thoracolumbar fractures. However, MSAC noted that the trial was also not powered to assess such interactions, only the primary outcome for the overall intention-to-treat population.

Among VAPOUR trial participants, about 30% had a thoracic fracture, 12–15% a lumbar fracture and 60% a thoracolumbar fracture. During the hearing, the representatives of the applicant stated that, from the subgroup analyses, the highest probability of best outcome was in thoracolumbar fractures of <3 weeks duration. They further suggested that variation in treatment effect by fracture site would be biologically plausible due to different flexibility and flexion forces across different sites. MSAC queried whether vertebroplasty should be confined to use in thoracolumbar fractures. The representatives of the applicant noted that meaningful benefit can also be achieved in patients with fractures in other locations. For example, if patients with vertebral degeneration and chronic lower back pain also have an acute lumbar fracture, the chronic pain will become worse if the acute pain is not addressed. Although improvement may not seem dramatic, it is still of benefit, but the VAPOUR trial was unable to assess this.

The representatives of the applicant sought to address MSAC's concerns regarding the choice of a 14-day timeframe after the intervention for achieving the primary outcome. During the hearing, the representatives of the applicant explained the importance of early pain relief to allow earlier mobilisation for these patients. Major complications related to vertebral fractures occur in the first few days if patients cannot be mobilised. Relief of their pain within 14 days allows them to return home. If patients are not remobilised early, they will continue to have deteriorated function and will not recover to previous health. Long-term outcomes

may include requiring aged care where they would otherwise have remained in their own home, or they may even die if pain is managed poorly in the first few weeks.

The representatives of the applicant sought to address MSAC's concerns related to the choice of the primary outcome itself. The reason stated by the representatives of the applicant for using a binary outcome rather than a continuous value was that it allowed the trial investigators to quantify the difference in how many patients achieved a pre-specified clinically important reduction in pain from severe to mild. The representatives of the applicant considered this to be a better indication of efficacy than a difference in the mean pain score between the randomised groups. The representatives of the applicant noted that, in analyses of the same trial results reported as mean pain scores, results following vertebroplasty were consistently better than those for controls and the differences in mean pain scores were maintained over time to 6 months.

MSAC acknowledged that there were valid reasons for choosing a primary outcome based on pain, but considered that evidence of functional improvements would also be of value given the arguments that early mobilisation of these patients is likely to lead to health improvements. MSAC noted that some of the secondary outcome measures in the VAPOUR trial (the timed up-and-go score and elements of the EQ-5D score) provided data on functional improvements, but showed no significant difference for vertebroplasty vs placebo.

MSAC also noted that, because the primary outcome was pain, there was the potential for unblinding. MSAC acknowledged that, although investigators could identify the sham procedure, outcome assessors were blinded to the nature of the procedure (sham or vertebroplasty). MSAC also considered that, because patients were under conscious sedation for the procedure, it would be unlikely they would be aware of which procedure they had when coming out of this sedation.

The representatives of the applicant sought to address claims in the Cochrane review that VAPOUR trial results were subject to detection bias. The representatives of the applicant clarified that patients were asked to guess which procedure they had and to give reasons for that guess. The representatives of the applicant noted that 80% of patients who had vertebroplasty guessed correctly and gave the reason as reduction in pain; 50% of the placebo group guessed correctly based on pain relief. No other reasons were reported. The representatives of the applicant claimed that there was no evidence of unblinding resulting from the questionnaire about blinding. The representatives of the applicant also noted that the approach to blinding in the VAPOUR trial was the same as in the Kallmes trial. MSAC concluded that the sham-controlled RCTs were all likely to have been affected by later unblinding, such that detection bias would probably not have been adequately minimised.

In terms of analgesic use, MSAC noted that there was no difference in short-term (up to 14 days) analgesic use between intervention and placebo groups. However, it is not known what analgesics (for example, opiates or paracetamol) or doses were received by patients across each group. MSAC also acknowledged that assessment of analgesic use in this population could also be confounded due to the prevalence of non-opiate analgesic use for other conditions, such as arthritis. During the hearing, the representatives of the applicant stated that there was no pre-specified pain management protocol; pain management was determined by the attending physician. The representatives of the applicant also stated that, because of the difficulty of ascertaining from patients the type of analgesic and/or the strength of dose, the pragmatic decision was made to only record whether analgesics were used or not. MSAC considered that non-standardised analgesic use and lack of detail about the type and dose used made it difficult to interpret the pain scores, including the impression

that the size of the effect on reducing pain appeared less than the size of the effect on reducing analgesic use.

MSAC formed the view that early-, medium- and long-term outcomes are likely to be different. MSAC considered that it would be valuable to have more information about long-term outcomes (6 months to 1 year).

MSAC noted the uncertainty inherent in extrapolating results for a small number of patients from the VAPOUR trial to the whole intended population in Australia, especially when most of the patients came from a single centre. MSAC considered that the small numbers in this trial and the nature of its primary outcome contributed to imprecise estimates of the magnitude of overall effect. MSAC also noted that about 15% of both intervention and placebo groups were lost to follow-up (6 of 36 who achieved the primary outcome at 6 weeks; 2 of 12 in the placebo group). MSAC considered this to be an important loss given the small number in the trial and with events, which contributed to the imprecision. MSAC acknowledged that this loss to follow-up also indicated the frailty of these intended patients.

MSAC noted statements by the representatives of the applicant that the VAPOUR trial should not have been included in the 2018 Cochrane review because it is clinically heterogeneous to other trials. The representatives of the applicant reiterated that the VAPOUR trial is the only blinded randomised trial directly meeting the initially proposed patient eligibility criteria. Differences highlighted by the representatives of the applicant included the proportion of hospital inpatients in the trial (VAPOUR 59% vs none in other blinded randomised trials), the fracture duration range (≤ 6 weeks vs 12 weeks to 12 months), the mean fracture duration (2.6 weeks vs 6.1–22.5 weeks), the baseline mean pain score (8.6 vs 7.0–7.8) and the polymethylmethacrylate (PMMA) bone cement volume used (7.5 mL vs 2.6–5.1 mL). The representatives of the applicant claimed that the VAPOUR and Yang et al trials are the only trials with evidence of benefit in acute fractures.

MSAC recalled that its November 2018 decision was primarily based on results of the VAPOUR trial, and MSAC considered that, in contrast to the assertions by the representatives of the applicant, the conclusion of the 2018 Cochrane review (that vertebroplasty does have a small benefit [7% improvement in mean pain score at 1 month]) was consistent with the VAPOUR trial results (claiming a 12% improvement in mean pain score at 14 days). MSAC considered that including the totality of evidence provides greater robustness to and generalisability of the clinical conclusions and decision-making rather than just relying on a single small trial with 85% of participants managed in a single centre. MSAC considered that the observed heterogeneity in outcomes across the trials in the Cochrane review appears to be no more than could be expected due to chance alone. MSAC rejected the notion that combining the VAPOUR trial with other studies was non-informative.

MSAC considered that an independent IPD-based meta-analysis of relevant trials could provide more informative clinical data on:

- estimates of effect based on all types of reported outcomes, not just reduction in pain, including
 - the binary pain outcome of the VAPOUR trial and exploring different thresholds of baseline pain and pain reduction in this definition
 - mean difference in pain outcomes
 - functional improvement/mobility and long-term outcomes
- potential harms, including
 - risk of subsequent refracture and/or adjacent fracture

- sources of clinical heterogeneity in predicting and estimating the extent of any treatment effect modification
 - fracture duration
 - baseline pain score
 - PMMA volume
 - patient eligibility determined in hospitalised patients or not
 - sham comparison or not
 - potential unblinding of outcomes in sham comparisons
 - site of fracture (thoracolumbar vs other sites).

MSAC noted that the IPD meta-analysis should include data from the Yang et al trial, about which more information would be needed.

During the hearing, the representatives of the applicant agreed that combining IPD that is homogeneous with VAPOUR data would be useful. However, the representatives of the applicant believed that, while it may be possible to control for duration of the fracture, it would not be possible to control for the patient cohort because of the differences in degree of osteoporosis and hospitalisation between VAPOUR and other trials, as well as differences in technique (cement volume) between trials. MSAC considered that the IPD meta-analysis could confirm the applicant's assertions that vertebroplasty is more effective in patients with the specific characteristics that were included in the VAPOUR trial (hospitalised patients with short fracture duration and more severe pain, using larger PMMA volumes) by providing more robust comparisons with results for patient characteristics not included in the VAPOUR trial. In other words, to better test the applicant's inferred hypotheses that each of these characteristics are treatment effect modifiers.

MSAC noted that its concerns raised previously remain about the economic evaluation. However, MSAC considered that more robust clinical results provided by an IPD-based meta-analysis could better inform the economic evaluation. However, MSAC also considered that even if the broader clinical issues could be dealt with by an IPD meta-analysis, some issues with the implausible utility estimates and extent of estimated cost offsets would still remain with the economic evaluation (for example, whether vertebroplasty results in fewer or shorter hospitalisations, and whether MRI is included as a cost for the comparator arm). These issues would need to be addressed separately to the proposed meta-analysis.

MSAC noted that the most recent (2011) utilisation data for the previous vertebroplasty item number had showed reducing levels of use before the item's removal from the MBS. However, since then, no quantitative utilisation data are available. The representatives of the applicant sought to address MSAC's concerns regarding leakage from a reintroduced MBS item. The representatives of the applicant noted that 59% of patients in the VAPOUR trial were inpatients and that the utilisation data for the previous vertebroplasty MBS item showed that 54% were inpatients. During the hearing, the representatives of the applicant claimed there is no evidence to suggest any leakage due to larger proportions of outpatients receiving vertebroplasty. However, the representatives of the applicant also stated that if patients can be seen early at home, in aged care facilities or in clinics, and treated with vertebroplasty if their pain does not improve within a few days, they could avoid hospitalisation for pain management.

MSAC considered that a stakeholder meeting would also provide valuable perspectives from both clinicians and patients. MSAC considered it important to seek the views of a broader group of clinicians, who treat the same fractures differently in different contexts as evidenced by the variation in use of the previous vertebroplasty MBS item across states and territories,

about the perceived clinical effect of vertebroplasty and the durability of that effect. Broader clinician input from other speciality types would also help to further define the group with greatest clinical need, and how and when best to assess these characteristics to determine those patients who are eligible, including exploring the option for a combined decision between a spinal surgeon and an interventional radiologist. Input from patients would also be of value to confirm the outcomes that are most important for elderly people with symptomatic spinal fracture, particularly over time and in relation to analgesic use and functionality. MSAC acknowledged that, given their frailty and immobility, it may be difficult for affected patients to attend a stakeholder meeting. However, MSAC considered that wider consumer engagement is also important and both perspectives could be provided by well-informed consumer/patient advocate groups/societies. The outputs of the stakeholder meeting may also help to better specify the questions for the IPD-based meta-analysis.

3. MSAC's advice to the Minister – November 2018 consideration

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC did not support public funding for vertebroplasty for severely painful osteoporotic vertebral fractures of less than either 3 or 6 weeks duration. MSAC considered that there may be a small clinical benefit, but MSAC was uncertain of its clinical significance, and that the cost-effectiveness is highly uncertain with substantial risk of use beyond the proposed patient population.

Summary of consideration and rationale for MSAC's advice – November 2018

At the hearing, the applicant noted ESC's concern that the clinical benefits of vertebroplasty were small, but asserted that the benefits were clinically significant. The applicant confirmed that no data were available after 6 months follow-up, and acknowledged that any long-term benefits would likely depend on the type and severity of the fracture.

MSAC noted that vertebroplasty was previously listed on the MBS as an interim-funded service (items 35400 and 35402) from 2005 to 2011. MSAC reviewed this service in April 2011 and did not support continued public funding based on two randomised sham-controlled trials (RCTs). MSAC considered that vertebroplasty had not been proven to be more effective than conservative treatment based on the available evidence. However, MSAC also noted uncertainties about the evidence at the time and accepted that vertebroplasty may have a role in the management of a subgroup of patients with acute, unstable vertebral fractures. Application 1466 was submitted following completion of a new clinical trial (VAPOUR) in 2016. The VAPOUR trial was a sham-controlled RCT conducted by the applicants.

The VAPOUR trial concluded that vertebroplasty is superior to sham intervention with regard to pain relief, functional disability and quality of life (QoL) up to six months post-intervention.

MSAC acknowledged that a small clinical benefit likely exists, but that the exact magnitude of the benefit appeared uncertain. MSAC noted that the primary clinical evidence provided was derived from one trial (the VAPOUR trial) and that, although four hospital sites were included in the trial, one of these sites treated approximately 84% of participants. MSAC expressed the concern that the results of this trial may not be generalisable to other settings.

MSAC noted ESC's observation that 80% of patients enrolled in the VAPOUR trial were treated within 3 weeks of fracture (mean time 2.6 weeks), resulting in the applicant proposing to restrict access to patients to fractures of 3 weeks duration or less. However, MSAC considered that 3 weeks may be insufficient time for patients to be referred to an appropriate

specialist and enter the clinical management pathway, which may create equity issues. Data from 2005 to 2011 (when vertebroplasty was listed on the MBS) showed large utilisation variation among the states and territories, suggesting equity of access was evident historically.

MSAC considered that the primary outcome in the VAPOUR trial of reduced pain was subject to detection bias, and the primary outcome and its timeframe of analysis being 14 days post-intervention did not appear to be justified. The applicant was unsure whether the trial had used the 3-level EQ-5D or the 5-level EQ-5D; MSAC considered this to be important because the 'pain and discomfort' domain is weighted differently (0.446 and 0.682, respectively) across these two versions of the EQ-5D instrument. Given the apparent benefit for pain, MSAC noted that the impact on the EQ-5D outcome was more modest than expected, and was time-dependent. For these reasons, MSAC had concerns about the translation of these results into the economic evaluation.

MSAC noted that both the intervention and the sham intervention showed a reduction in pain scores post-intervention. MSAC noted that the nominated clinically significant numeric rating scale (NRS) change was 35%, or 3.8 points on an 11-point scale, which was only surpassed on day 3 post-intervention in the VAPOUR trial. MSAC was concerned about the use of the NRS rather than the visual analogue scale (VAS), and that the evidence from other trials used both NRS and VAS, making comparisons difficult. MSAC acknowledged that the vertebroplasty group did have significantly lower analgesic use than the sham group, suggesting that these patients experienced greater reductions in pain.

MSAC was also concerned that a loss of blinding could have contributed to the results from the VAPOUR trial. MSAC queried why some patients were lost to follow-up at similar rates across the two groups over time, with up to 15% (102/120) patients not included in the final data analysis.

MSAC compared the results of the Cochrane review with those of the VAPOUR trial alone. MSAC acknowledged the differences across the trials used (intervention, comparator, outcome), but noted low heterogeneity in the results observed among all trials. MSAC therefore advised that it had moderate confidence that there is a small benefit, but this is of uncertain clinical significance and it had low confidence in the magnitude of the benefit. From this overall assessment, MSAC further advised that it had low confidence that the age of fracture is a treatment effect modifier, including the post-hoc subgroup analysis reported in the VAPOUR trial varying this time period from 6 weeks to 3 weeks.

MSAC noted the high likelihood of leakage, particularly from the inpatient setting of most of the patients in the VAPOUR trial, which would lead to increased costs and unacceptable incremental cost-effectiveness ratios (ICERs) due to their heavy reliance on hospital cost offsets in which MSAC had low confidence. MSAC also had low confidence in the extrapolation from 6 months to 1 year, noting that the results up to 6 months suggested an attenuating effect over time.

MSAC considered that, given the likelihood that vertebroplasty has a small benefit but the magnitude and clinical significance is uncertain, further studies may be best focused on the use of vertebroplasty based upon outcomes of critical importance to patients and clinicians. This may include duration of hospitalisation. The hearing discussed the possibility that treatment with vertebroplasty may allow mobilisation and early discharge in a select group of patients who have been admitted to hospital within a few weeks of acute fracture. Such a randomised trial would need to be undertaken at multiple sites to ensure sufficient size and

generalisability. MSAC could refer this study for the consideration of Medical Research Future Fund.

4. Background

Vertebroplasty was previously listed on the MBS as an interim funded service (items 35400 and 35402) from 2005 to 2011. MSAC reviewed this service in April 2011, and did not support continued public funding.

5. Prerequisites to implementation of any funding advice

The prostheses required for this procedure are on the Prostheses List. The devices listed below are all inclusive of PMMA cement and an associated delivery system (Table 1). Additionally, consumables required for the intervention are skin antiseptic, sterile drapes, sterile gown and gloves for the operator. No follow-up imaging or treatment is routinely given after vertebroplasty (Table 1).

Table 1 Vertebroplasty devices listed on the Prostheses List

Name	Code	Description	Minimum benefit
G-21 Kit	OH503	Radiopaque Bone Cement for Vertebroplasty	\$500.00
Vertebroplasty System	JJ609	Vertebroplasty System	\$174.00
Traumacem	SY429	Cement with mixing and delivery system	\$500.00
AVAmox	HW577	Radiopaque bone cement system	\$500.00

The application proposed that the service would be exclusively used in the hospital setting for the treatment of severe pain due to osteoporotic vertebral fracture that had not responded to medical management.

6. Proposal for public funding

The applicant proposed amending the item descriptor to restrict the proposed population to fractures of 3 weeks duration or less (Table 2).

Table 2 Proposed MBS item descriptor

Category 3—therapeutic procedures
<p>VERTEBROPLASTY, performed by an interventional radiologist, for the treatment of a painful osteoporotic vertebral compression fracture, where</p> <ul style="list-style-type: none"> a) pain is severe (numeric rated pain score ≥ 7 out of 10); b) symptoms are poorly controlled by analgesic therapy, namely opiates; c) severe pain duration is <6 weeks ≤ 3 weeks; and d) there is MRI (or SPECT-CT if MRI unavailable) evidence of acute vertebral fracture. <p>Not to be performed more than once on the same fracture. (Anaes.) MBS Fee: \$700</p>

7. Summary of Public Consultation Feedback/Consumer Issues

23 responses were received in the consultation feedback.

Two professional organisations supported the application. One organisation highlighted the importance of appropriate inclusion and exclusion criteria to identify suitable patients for the service. The other organisation provided similar feedback noting the service would benefit a selected group of patients.

Of the 18 individual professionals or collective groups, 13 were supportive and five were not or had reservations. Most supported responses highlighted the reduction in pain and improved mobility as being the primary benefits of the proposed service. The most frequently raised disadvantage was associated with complications arising from poor skill and training of the treating clinician. Linked to this, three responses raised concerns about the complications arising from extravasation of cement. The responses that were not supportive or had reservations identified a paucity of evidence of benefit or the risk of complications as their reason for their response. The respondents do not expand upon these statements, so it is not possible to include further detail in this summary.

One response proposed that initial assessment should be performed by a spinal surgeon rather than an interventional radiologist; and another two responses proposed that the item should also be available to pain specialists. Three responses raised concerns about potential overuse of the service once listed.

Two patients who had received the service were supportive.

A device manufacturer supported the application for MBS subsidy of vertebroplasty to allow access to this therapy in a private setting.

8. Proposed intervention's place in clinical management

The application stated that, if vertebroplasty were to be publicly funded, it would be added to conservative medical therapy for patients with a confirmed acute osteoporotic vertebral compression fractures (OVCF), with poor pain control and poor function, where there is no morphologic contraindications to vertebroplasty (Figure 1). Patients not fitting these criteria would continue to receive conservative medical therapy alone.

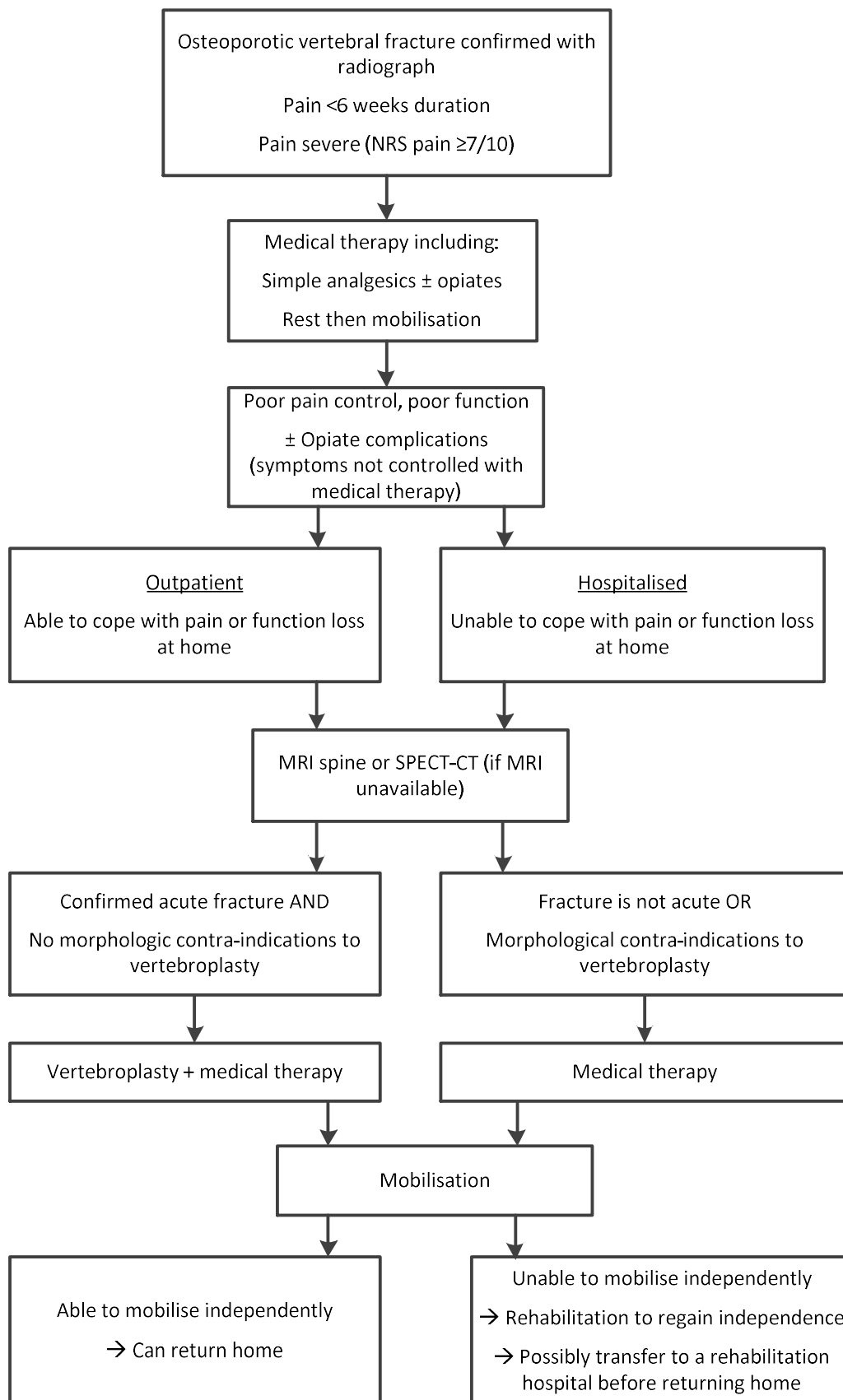


Figure 1 Clinical management algorithm for the proposed new intervention

MRI = magnetic resonance imaging; NRS = numeric rating scale; SPECT = Single-photon emission computed tomography

9. Comparator

The application nominated intensified and extended conservative medical therapy as the comparator.

10. Comparative safety

The application presented five randomised controlled trials (RCTs), two non-randomised studies, and three case series studies. Safety outcomes reported in the included studies were new fracture incidence, cement leakage, other adverse events, and mortality.

From the limited evidence available, the procedure-related adverse events associated with vertebroplasty appear to be infrequent and mild. Due to the limited availability of long-term follow-up data in the proposed population, the long-term risks of vertebroplasty in relation to mortality, cement leakage, new fractures, and other adverse events are uncertain.

The application claimed that vertebroplasty has non-inferior safety compared to conservative medical therapy.

11. Comparative effectiveness

Pain was measured as the primary effectiveness outcome in all of the included trials. The VAPOUR trial reported that vertebroplasty significantly reduced severe pain in a greater proportion of patients who had acute OVCFs. This treatment effect was most substantial at day three, and then sustained over the whole trial period (six months).

Table 3 VAPOUR treatment effects of vertebroplasty for patients with fractures ≤6 weeks old

Follow-up	Day 3	Day 14	Month 1	Month 3	Month 6
Proportion of patients with NRS pain score <4					
Vertebroplasty n/N (%)	18/58 (31)	24/55 (44)	28/55 (51)	29/53 (55)	35/51 (69)
Placebo n/N (%)	5/55 (9)	12/23 (21)	10/57 (18)	17/52 (33)	24/51 (47%)
Difference (95% CI)	22 (8, 36)	23 (6, 39)	33 (17, 50)	22 (4, 41)	22 (3, 40)
p-value	0.004	0.011	0.0002	0.023	0.027
Reduction in NRS pain score					
Vertebroplasty mean (SD)	3.5 (2.6)	4.2 (2.7)	4.6 (3.0)	5.4 (3.5)	6.1 (3.3)
Placebo mean (SD)	1.8 (2.3)	3.0 (3.0)	3.2 (2.7)	4.1 (3.1)	4.8 (3.1)
Difference (95% CI)	1.8 (0.8, 2.7)	1.2 (0.1, 2.3)	1.4 (0.4, 2.5)	1.3 (0, 2.6)	1.3 (0, 2.6)
p-value	0.0003	0.026	0.010	0.047	0.043
Reduction in RDQ score					
Vertebroplasty mean (SD)	4.5 (6.2)	5.9 (5.8)	6.9 (6.0)	9.6 (7.7)	11.7 (6.5)
Placebo mean (SD)	2.9 (4.4)	4.1 (6.3)	4.3 (5.6)	6.4 (7.0)	7.4 (6.9)
Difference (95% CI)	1.6 (0.4, 3.6)	1.8 (0.5, 4.1)	2.6 (0.4, 4.8)	3.2 (0.3, 6.1)	4.2 (1.6, 6.9)
p-value	0.111	0.121	0.021	0.031	0.0022

The results from the four supplementary trials of vertebroplasty were variable. Two out of four studies showed no significant benefit related to vertebroplasty, while the other two studies found vertebroplasty to offer superior pain relief.

Vertebroplasty may be more effective for some patients (e.g. when used soon after presentation with acute OVCF). However, considering the entire population enrolled in the VAPOUR trial, the variation in treatment effect is uncertain.

Overall, the application claimed that vertebroplasty has superior effectiveness compared to conservative medical therapy in relation to pain relief.

Clinical claim

The application claimed that vertebroplasty has superior effectiveness compared to conservative medical therapy in relation to pain relief, and non-inferior safety.

12. Economic evaluation

The application presented a cost-utility analysis to determine the value of vertebroplasty for severely painful OVCF of less than 6 weeks duration compared to conservative medical therapy (Table 4).

Table 4 Summary of the economic evaluation

Summary of the economic evaluation	
Perspective	Health system
Intervention	Vertebroplasty performed in a non-mobile fluoroscopy suite
Comparator	Conservative medical therapy
Type of economic evaluation	Cost-utility analysis
Sources of evidence	Randomised controlled trial in Australia; systematic review of economic evaluations
Time horizon	6 months in the model base case, 1 year in stepped analyses
Outcomes	QALYs
Methods used to generate results	Cohort expected value analysis
Health states	Alive, Dead
Cycle length	1 week
Discount rate	5% used for base and 3.5% and 7% sensitivity analyses
Software packages used	Microsoft Excel 2010

QALY = quality-adjusted life year

The economic analysis was modified to remove the cost of magnetic resonance imaging (MRI) from the conservative therapy arm (Table 5).

Table 5 Economic model of vertebroplasty for vertebral fractures, with or without MRI cost in conservative therapy

	Cost	Incremental cost	QALYs	Incremental QALYs	ICER/QALY
6 months					
Vertebroplasty	\$10,118.32		0.37		
Conservative therapy with MRI	\$10,282.54	\$-5.52	0.35	0.02	Dominant
Conservative therapy without MRI	\$9,765.44	\$352.88	0.35	0.02	\$16,104.57
1 year					
Vertebroplasty	\$10,574.09		0.73		
Conservative therapy with MRI	\$10,737.14	\$-163.05	0.70	0.04	Dominant
Conservative therapy without MRI	\$10,378.74	\$195.35	0.70	0.04	\$5,331.51

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; MRI = magnetic resonance imaging

13. Financial/budgetary impacts

An epidemiological approach was used to estimate the financial implications of the reintroduction of vertebroplasty for OVCF. The financial estimates were presented including (and removing) the cost of MRI from the cost of conservative medical therapy.

Table 6 Financial impact of vertebroplasty with or without the cost of MRI in conservative therapy

	2019	2020	2021	2022	2023
Vertebroplasty cost to the MBS	\$158,977	\$258,103	\$361,706	\$370,025	\$378,536
Conservative cost to the MBS with MRI	\$0	\$67,752	\$138,620	\$141,808	\$145,070
Conservative cost to the MBS without MRI	\$0	\$54,108	\$110,704	\$113,250	\$115,855
Net cost to the MBS	2019	2020	2021	2022	2023
Net MBS cost with MRI used in conservative therapy	\$158,977	\$190,352	\$223,086	\$228,217	\$233,466
Net MBS cost without MRI used in conservative therapy	\$158,977	\$203,996	\$251,002	\$256,775	\$262,681
Cost difference	\$0	-\$13,644	-\$27,916	-\$28,558	-\$29,215
Net cost to the state and territory health budget	2019	2020	2021	2022	2023
Net health budget cost with or without MRI	\$3,501,839	\$3,582,382	\$3,664,776	\$3,749,066	\$3,835,295

MBS = Medicare Benefits Schedule; MRI = magnetic resonance imaging

14. Key issues from ESC for MSAC

Key issues from ESC to MSAC - *October 2018*

ESC key issue	ESC advice to MSAC
Evaluation of Cochrane review (the Critique)	The applicant-commissioned Critique deemed that the Cochrane review has limited relevance to the current MSAC assessment due to critical errors in the subgroup analysis of fractures of ≤ 6 weeks duration, and its assessment of bias of included studies. The main weakness of the Cochrane review was identified as being its misalignment with the population proposed in the new PICO criteria for Application 1466 (patients with fracture duration of ≤ 3 weeks).
VAPOUR trial is the most appropriate for the revised PICO	The VAPOUR trial was the only blinded trial to require severe pain (NRS $\geq 7/10$) despite analgesic therapy (including opioids), to limit fracture duration to ≤ 6 weeks (with most participants having a fracture duration ≤ 3 weeks) as inclusion criteria, and to include hospitalised inpatients. This may explain the claimed larger effect size reported by the VAPOUR trial compared to others. All other blinded trials excluded hospitalised inpatients and included a significant proportion of patients with fractures of a longer duration.
Inclusion criteria of studies in the Cochrane review and applicability to new PICO criteria	The Cochrane review had relatively broad inclusion criteria. There was a substantial level of heterogeneity between studies, especially in terms of pain duration, baseline pain and cement volumes. Overall, VAPOUR had more stringent patient selection than the other trials.
Inconsistency between the VAPOUR population and most other blinded RCTs	It may be inappropriate to meta-analyse multiple datasets (as done in the Cochrane review). However, this conclusion assumes the use of vertebroplasty is limited to a very tightly defined population, consistent with the majority of participants in the VAPOUR study.
Determining whether treatment effect is clinically meaningful	Reduced hospitalisation/length of stay may be a more appropriate outcome to measure than pain scores as a proxy for treatment effect.
Cut-off for fracture duration	Three weeks may not be a feasible timeframe for patients to get through the normal referral pathway and to have sufficient time to test whether opioids are successful. Limiting fracture duration to 3 weeks may have implications for access to vertebroplasty.
Uncertainty around hospital services as a key driver of incremental cost and ICER	All base case assumptions for hospital inpatient costs (proportion of patients hospitalised at baseline, cost per additional hospital day, and difference in length of stay) favour vertebroplasty. The multivariate sensitivity analysis (ICER \$71,000/QALY) would be a more appropriate respecified base case.

ESC discussion

ESC recalled the previous considerations of vertebroplasty and noted changes made by the applicant to the original submission previously considered by ESC in February 2018 and June 2018. ESC noted that the Department of Health had agreed that the amendment could be considered as part of the current application (Table 2).

ESC noted that evidence for the safety and efficacy of vertebroplasty should therefore reflect a population with acute osteoporotic fractures (≤ 3 weeks duration) and severe pain (pain score ≥ 7 on Visual Analogue Scale [VAS] or Numerical Rating Scale [NRS]) despite analgesic therapy (opioids), including hospitalised inpatients. ESC noted that the applicant-commissioned Critique of the contracted reports assessed the relevance of evidence for the efficacy of vertebroplasty against these criteria, as well as limiting eligible studies to randomised controlled trials (RCTs) comparing vertebroplasty to either placebo or conservative therapy.

ESC noted the key sources of evidence considered in the Critique:

- two systematic reviews assessing the efficacy and safety of vertebroplasty in patients with osteoporotic vertebral fractures
 - the contracted assessment for Application 1466
 - the Cochrane review (Buchbinder et al. 2018)
- an individual patient data (IPD) meta-analysis (Staples et al. 2011) from two sham-controlled RCTs of vertebroplasty undertaken by
 - Kallmes et al. 2009
 - Buchbinder et al. 2009.

ESC noted that the Staples meta-analysis included data from a subgroup of patients with pain of recent onset (≤ 6 weeks) or severe pain (score ≥ 8 on 0–10 NRS).

ESC noted the conclusion of the contracted assessment that vertebroplasty is superior to sham intervention for pain relief, functional disability and quality of life up to 6 months, based primarily on the results of the VAPOUR trial. Maximum pain reduction was achieved at the earliest follow-up (day 3), and the benefit tended to stabilise after 3 months. Maximum between-group difference in NRS pain scores was 1.8 at 3 days, and the difference remained at 1.3 at 6 months.

ESC noted that the contracted Commentary to consider the implications of the Cochrane review for the contracted assessment reported that benefits from vertebroplasty are primarily gained by day 3, with additional proportions of responders roughly equivalent across the vertebroplasty and sham comparator arms from then until 6 months follow-up.

ESC noted that the Critique concluded that ‘this observation simply suggests that vertebroplasty has an early effect on pain relief and this incremental effect is maintained through follow-up’. ESC queried this conclusion, noting that although vertebroplasty may have an earlier effect on pain than sham intervention, the difference in effect may not be maintained over time.

ESC noted the uncertainties in effectiveness data in the contracted assessment. ESC noted that the benefit seemed relatively small (score differences between the two arms of < 2) and that NRS and VAS results did not demonstrate a consistent outcome.

ESC noted that the contracted assessment concluded that fracture duration and severity of pain at baseline were likely to be important effect modifiers. ESC recalled its previous

observation that 80% of patients treated in the VAPOUR trial had a fracture age ≤ 3 weeks. ESC noted results of a subgroup analysis of the primary outcome according to fracture age (≤ 3 weeks, >3 weeks) undertaken in the Critique. At day 14, there was no difference in the proportion of patients with an NRS pain score of <4 among the 86 patients with fractures of ≤ 3 weeks duration compared to the 24 patients with fracture age >3 weeks ($p = 0.12$). ESC noted that no conclusions can be drawn from this subgroup analysis because of the small number of patients in the VAPOUR trial with fracture duration of >3 weeks. ESC noted, however, that the Critique concluded there was a trend to enhanced benefit in the subgroup with fracture duration ≤ 3 weeks.

ESC noted the contracted assessment conclusion that vertebroplasty had inferior safety to conservative medical therapy, which is expected considering vertebroplasty involves an operation. ESC noted that although most adverse events associated with the intervention are mild, and severe adverse events are rare, the risk of cement leakage poses an additional risk compared with conservative management.

ESC noted effectiveness data from the Cochrane review of vertebroplasty (Buchbinder et al. 2018). The Cochrane review judged the evidence to be of high to moderate quality and concluded that there were no demonstrable clinically important benefits of vertebroplasty compared to placebo (sham procedure). ESC noted results from the Cochrane review showing that the mean pain score (on a 1–10 scale) was only 0.6 points better for vertebroplasty than for placebo (which had a mean score of 5 points). The Cochrane review also showed an absolute pain reduction of 6% (compared to a minimum clinically important difference of 15%) and a relative pain reduction of 9% (based on five trials with 535 participants). The review claimed that heterogeneity in results of different trials could be ascribed to a higher risk of bias in the VAPOUR trial.

ESC noted that the Cochrane review found that fracture age was not an effect modifier. Subgroup analysis indicated that results did not differ according to duration of pain (≤ 6 weeks versus >6 weeks). ESC noted, however, that Commentary reported errors in the subgroup analysis and suggested that the IPD meta-analysis by Staples et al. (2011) was likely to be more reliable.

ESC noted the safety results of the Cochrane review. The review found the evidence to be of moderate quality (from seven trials with up to 24 months follow-up). The review concluded that there was insufficient evidence to determine whether vertebroplasty increases the risk of new symptomatic vertebral fractures, and that the relationship between vertebroplasty and serious adverse events is uncertain.

ESC noted the statement in the Critique that serious adverse events related to conservative therapy, including fracture instability and opioid side effects, were listed in the PICO, but were not discussed by the contracted assessment or the Cochrane review.

ESC noted the results of the Staples et al. (2011) meta-analysis which investigated the impact of fracture age on the clinical benefit from vertebroplasty. This was a meta-analysis of subgroups of patients with acute fractures (≤ 6 weeks) or NRS pain at baseline ≥ 8 from the Kallmes et al. (2009) and Buchbinder et al. (2009) sham-controlled trials.

ESC noted that results of the meta-analysis did not support the hypothesis that selected subgroups would benefit from vertebroplasty; results showed there was no advantage of vertebroplasty over placebo for participants with recent onset fracture or severe pain (based on between-group differences in pain and disability scores).

ESC noted the Critique's argument that the meta-analysis was not powered to detect a pain difference of 1.5 on a scale of 1–10 (i.e. the minimum clinically important difference). An adequately powered study would require at least 120 patients; the meta-analysis included only 25 patients in the vertebroplasty arm and 32 receiving placebo. Results of the meta-analysis should therefore be interpreted with caution.

ESC noted the Cochrane review included five trials – Buchbinder et al. (2009), Clark et al. (2016; the VAPOUR study), Kallmes et al. (2009), VERTOS IV and VOPE (2015). It also included an additional subgroup analysis by fracture duration (≤ 6 weeks versus > 6 weeks) that included the same trials except VOPE (2015), with subgroup data from the trials by Buchbinder et al. (2009) and Kallmes et al. (2009).

The contracted assessment had much more strict inclusion criteria that aligned with the ratified PICO criteria (RCTs where the mean or median fracture duration was ≤ 6 weeks, and the mean or median baseline pain severity was ≥ 7 on a rating scale of 1–10); the only eligible study was the VAPOUR trial by Clark et al. (2016). Several other RCTs which included slightly broader populations were considered 'supplementary' evidence (Rousing et al. 2009, VERTOS II, VERTOS IV, Yang et al. 2016).

ESC noted that the Cochrane subgroup analysis, the contracted assessment and the Staples IPD meta-analysis each relied on a different set of studies to arrive at their conclusions about the clinical efficacy of vertebroplasty. ESC noted the Critique's comment that the validity of these analyses depends on the applicability of each study to the population proposed for reimbursement on the MBS, and whether meta-analysis of these data is appropriate.

ESC noted the Critique's comments on the applicability of studies included in the Cochrane review. ESC noted that the Cochrane review based its findings most heavily on meta-analysis of the blinded (sham- or placebo-controlled) RCTs. The Critique noted that:

- the included trials varied in terms of pain duration, from ≤ 6 weeks (VAPOUR) up to < 12 months (Buchbinder et al. 2009 and Kallmes et al. 2009), and about 12 weeks in the VERTOS IV study (the Cochrane review, and the Commentary, incorrectly stated that the VERTOS IV study included patients with fracture duration < 6 weeks; importantly, at least 80% of patients in VERTOS IV had fractures of > 3 weeks)
- the duration of measured pain varied across studies (mean duration of pain in weeks), from 2.8 weeks (VAPOUR) up to 16 weeks (Kallmes et al. 2009) and 17.9 weeks for the subgroup with severe pain (≥ 8) in the Staples (2011) meta-analysis
- baseline pain scores (inclusion criteria) varied across studies, from ≥ 3 out of 10 (Kallmes et al. 2009) up to ≥ 7 out of 10 (VAPOUR); Buchbinder et al. (2009) had no restriction for baseline pain score
- the actual mean baseline pain scores in trials were similar, but VAPOUR had a higher mean baseline pain score than Buchbinder et al. (2009), VERTOS IV and Kallmes et al. (2009)
- mean baseline pain scores differed in the two subgroup analyses within Staples (2011) – the subgroup with shorter pain duration (< 6 weeks) had a lower mean baseline pain score than the subgroup with severe pain; in the subgroup of patients in VAPOUR with fracture duration ≤ 3 weeks, the baseline pain scores were similar to those in the intention-to-treat population
- different trials used different methods of administering the sham procedure – VAPOUR involved subcutaneous local anaesthetic injection which better reflects conservative therapy, minimising response in the placebo arm; other RCTs used periosteal local

anaesthetic which is an active control treatment that could itself relieve secondary facet joint pain

- patient selection criteria differed between trials, and therefore so too did consistency with the proposed MBS item descriptor – VAPOUR had more stringent patient selection than the other studies; all patients had fracture ages of <6 weeks, 80% had fractures of ≤ 3 weeks duration (consistent with the revised MSAC item descriptor), and VAPOUR also included both outpatients (41%) and inpatients (59%).

The only other RCT with fracture duration ≤ 3 weeks is Yang et al. (2016). This trial was not blinded, so was not included in Cochrane review subgroup meta-analyses 8.1 or 8.2 examining shorter fracture duration, but was considered supplementary evidence in the contracted assessment. Results demonstrated a significantly greater improvement in the VAS in the vertebroplasty arm from day 1, which was durable to 1 year (12-month mean difference = 1.2, $p < 0.001$).

ESC noted the Critique and Commentary AMSTAR2 ratings of the Cochrane review, restricted to aspects of the review that are relevant to the revised research question (i.e. the efficacy of vertebroplasty in a population with uncontrolled pain due to fractures of ≤ 3 weeks duration, compared to a sham intervention). ESC noted that the Commentary on the Cochrane review assigned an overall high AMSTAR2 rating, however, scored the review ‘low’ on one domain (appropriate methods for statistical combination of results). According to AMSTAR2 guidance by Shea et al. (2017), not meeting this criterion is considered a critical weakness in a systematic review. ESC noted that one critical flaw means the overall confidence in the results of the systematic review is low.

ESC noted that the Critique considered the Cochrane review of critically low quality as two critical and two non-critical domains were not met. The first critical flaw was that data included in the meta-analyses were a mix of final values and change from baseline values; there were also errors in the subgroup meta-analyses (8.1 and 8.2) for patients in the ≤ 6 weeks group. The second critical flaw related to the assessment of bias in the VAPOUR study.

The Cochrane review suggested that the high proportion of patients (over 50%) who could guess their treatment allocation suggested inadequate blinding, however, noted that it is possible that patients could guess which intervention they received because of treatment efficacy. ESC noted that pain was self-reported in the VAPOUR study. It is therefore also possible that the patients who thought they had received the treatment reported less pain.

ESC noted that the first domain of the AMSTAR2 checklist is also relevant to an assessment of review quality (i.e. did the research questions and inclusion criteria for the review include the components of PICO?) If the PICO criteria are not applicable to the research question of interest, then all other domains of the AMSTAR checklist are redundant. ESC noted that the population of interest in the Cochrane review (‘adults with painful osteoporotic vertebral fractures’) is not applicable to the PICO criteria for the current application (either ≤ 6 weeks or ≤ 3 weeks), and, therefore, the results of the systematic review for the wider population will not be applicable, and the partially applicable ≤ 6 weeks subgroup meta-analysis was flawed.

ESC noted that there seems to be a clear treatment effect due to vertebroplasty, but it remains unclear whether there is a difference in treatment effect depending on duration of the fracture (≤ 3 weeks vs > 3 weeks). ESC also noted that the effect is very small in terms of QALY incremental benefit, and that whether that effect is clinically meaningful has not been discussed.

ESC noted that because these patients have debilitating pain, perhaps a small treatment effect is enough for them to be able to leave hospital and self-manage their condition at home, and this would be a tangible benefit for them. ESC noted, however, that trials have not been designed to measure changes in hospitalisation. ESC proposed that reduced hospitalisation or length of stay may be a more appropriate outcome to measure than pain scores as a proxy for a patient-relevant and meaningful treatment effect.

ESC recalled that limiting the population to those with fractures of <3 weeks duration was in response to ESC comments in February 2018 regarding the high proportion of patients in the VAPOUR trial with fractures of this duration. However, ESC queried whether limiting the fracture duration to <3 weeks may create issues for access to vertebroplasty. It may not be a feasible timeframe for community-based patients to get through the normal referral pathway and to test whether opioids are successful. ESC noted that more than half the patients in the VAPOUR trial were inpatients.

ESC noted that there have been no changes to the economic evaluation since the application was last considered by ESC in February and June 2018. ESC noted that the economic evaluation was a cost-utility analysis comprising a within-trial economic evaluation (VAPOUR trial) and a model-based evaluation (but this was noted as redundant due to its simple structure).

Regarding the within-trial economic evaluation, ESC reiterated that:

- while vertebroplasty dominated conservative care in the base case, the incremental changes driving this finding were small
- assumed savings for hospital inpatient costs (proportion of patients hospitalised at baseline, reduction in hospital length of stay and cost per additional day of hospital stay) were a key driver of the economic model
- univariate sensitivity analyses varying these inputs (using plausible values) changed the results of the economic evaluation from dominant to an incremental cost-effectiveness ratio (ICER) of up to \$40,000 per QALY
- varying all three inputs at the same time (multivariate sensitivity analysis) resulted in an ICER of \$71,000 per QALY
- varying the proportion of outpatients from 0% to 30% (assuming a lower length of stay of 4 days and using a more appropriate marginal cost of \$566 per additional day of hospital stay instead of \$850) increased the ICER from \$15,000 per QALY to \$47,000 per QALY
- the costs of magnetic resonance imaging (MRI) should be removed from the conservative treatment arm of the model.

In summary, ESC noted that the key economic issues related to uncertainty around hospital services as a key driver of incremental cost and the ICER, and suggested that a multiple changes are needed to provide a more appropriate base case.

15. Other significant factors

Nil.

16. Applicant's comments on MSAC's Public Summary Document

This application is for elderly patients with severe pain, whose plight may have been overlooked by the MSAC. A typical patient is an 80 year old woman with severe pain from vertebral fracture less than 3-weeks old. She can't mobilise because getting out of bed hurts too much. She's lost functional independence and is hospitalised. She's taking both sustained release and short acting opiates, causing confusion and constipation but not controlling the pain. Vertebroplasty fills the vertebral body with PMMA, stabilising the fracture, stopping vertebral collapse, and reducing pain, allowing early mobilisation and hospital discharge. The alternative of bed rest and high dose opiates is toxic for old patients. Data for 93 patients in the VAPOUR trial with fractures less than 3-weeks duration, provided to MSAC, shows one month after vertebroplasty 55% of patients had low pain scores compared to 16% following placebo. The only other randomised trial to use vertebroplasty for uncontrolled pain within 3 weeks of fracture is the Yang2016 trial which is also strongly positive. The MSAC has granted equal weighting to three negative trials in a different patient group with older fractures and less severe symptoms which are irrelevant to this application. Elderly inpatients with the worst pain in their life are required to fund vertebroplasty themselves, even despite private health insurance, which is unfair. Further information is available from [<http://www.irsa.com.au/news/222-vertebroplasty> MSAC application 1466].

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)