NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

iFuse implant system for treating chronic sacroiliac joint pain

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in yellow. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Decision problem from scope

1 The technology

The iFuse implant system (SI-Bone) is intended for use in people with sacroiliac joint (SIJ) dysfunction. It consists of a sterile, cannulated titanium implant and a surgical instrument system for implantation. The implant has a triangular shape which is designed to limit lateral and rotational movement and shear stresses around the implant and has a porous metal coating which aims to facilitate bone-on-bone growth. The iFuse procedure requires a skin incision, muscle dissection, guide wire placement, drilling and broaching of bone, as well as placement of multiple implants. Typically 3 implants are used per joint depending on the size of the pelvis.

The iFuse implant system was CE marked as a class IIb medical device in 2010; the instruments comprising the instrument system are class I and class IIa devices.

2 Proposed use of the technology

2.1 Disease or condition

SIJ dysfunction can result from either intra-articular causes, for example arthritis or infection, or trauma including fractures. Low back pain can present with different levels of severity – for example, some people may be able to continue to work and lead active lives, while others may be severely disabled or unable to work.

2.2 Patient group

It is estimated that the prevalence of SIJ pain in people presenting with lower back pain ranges from 15% to 30%. SIJ dysfunction is generally treated in a stepped approach and less invasive treatments are used first. If these treatments are unsuccessful SIJ fixation surgery may be done.

2.3 Current management

The current standard of care for people with chronic SIJ dysfunction consists of escalating non-surgical treatment, typically beginning with non-steroidal

anti-inflammatory medications and/or opioids and physiotherapy. People with SIJ pain will be referred by their GPs to a physiotherapist for this treatment. If there is no improvement in pain in response to first-line measures, more invasive procedures are considered, typically steroid injections in the SIJ followed by radiofrequency ablation. If these measures are inadequate, SIJ fusion would then be considered. This can be done in a minimally invasive way with iFuse or through open surgery and is carried out by orthopaedic surgeons in tertiary centres.

NICE has published interventional procedures guidance on the procedure of which iFuse is a potential component; minimally invasive SIJ fusion surgery for chronic sacroiliac pain. The guidance recommends that the evidence supporting the procedure is adequate for it to be carried out with standard arrangements for clinical governance, consent and audit. The guidance further recommends that the procedure should only be done in people with a confirmed diagnosis of unilateral or bilateral SIJ dysfunction due to degenerative sacroilitis or SIJ disruption.

NICE guideline, Low back pain and sciatica in over 16s: assessment and management, refers to spinal fusion in general and states that there is insufficient evidence to support clinical or cost benefits. However the evidence considered in the guideline comparers spinal fusions with disc replacements and so are unlikely to involve the SIJ.

2.4 Proposed management with new technology

iFuse would be used in people with SIJ dysfunction in whom non-surgical management steps have failed to control symptoms, as an alternative to other surgical interventions.

3 Company claimed benefits and the decision problem

These are described in the scope here (link to Appendix E). The company proposed minor changes to the comparators, outcomes and subgroups in the

decision problem table of their evidence submission. These changes are described in the following table.

Table 1: Variations to the decision problem proposed by the company

Decision problem	Variation proposed by company	EAC view of the variation
Comparators	Added 'radiofrequency ablation'	The EAC felt that radiofrequency ablation was already covered under 'SIJ denervation'.
Outcomes	Added 'medication (opioid use)'	The EAC felt that all medications were covered under 'back/SIJ pain relief (including medicine use and post-operative pain scores)'.
Subgroups	Changed 'previous lumbar surgery' to 'previous spine lumbar surgery'.	The EAC felt that this clarification was justified.

4 The evidence

4.1 Summary of evidence of clinical benefit

The EAC included 12 studies in its evidence review. These studies comprise 2 randomised clinical trials (RCTs), 2 comparative studies and 8 non-comparative studies. All studies are published and were accessed as full papers. The rationale for the selection of these studies is in section 2 of the AR.

Table 2: Summary of evidence base

Study	Type of study	Comment
Studies included by both EAC and company: 11 studies	2 RCTs, 2 comparative studies and 7 non-comparative studies	RCTs: Polly et al. 2016a, Dengler et al. 2017b Comparative studies: Spain and Holt 2017, Vanaclocha et al. 2018 Non-comparative studies: Bornemann et al. 2017, Cher et al. 2015, Miller et al. 2013, Rudolf and Capobianco 2014, Sachs et al.

		2016, Duhon et al. 2016, Capobianco and Cher 2016
Studies presented by company and excluded by EAC: 17 studies	9 RCTs, 3 comparative studies, 1 case series study, 3 reviews and 1 *in vitro* study	8 RCTs (Polly et al. 2015, Whang et al. 2015, Dengler et al. 2016, Sturesson et al. 2017, Duhon et al. 2013 and 2016, Cher and Polly et al. 2016) were excluded as they reproduce results from other included studies. 1 RCT was excluded because it was not relevant to the decision problem. All 3 excluded comparative studies (Smith et al. 2013, Ledonio et al. 2014a and 2014b) and 1 excluded case series study (Vanaclocha et al. 2014) reproduce results from other included studies. 3 reviews were excluded by the EAC as results for iFuse are not listed separately. 1 *in vitro* study was excluded as it was not relevant to the decision problem.
Studies not in submission included by EAC: 1 study	1 case series study	1 case series study that had been mentioned but excluded by the company was included by the EAC as it reports outcomes for people who have had previous spine surgery.

The EAC noted that there was considerably more evidence comparing the use of iFuse with conservative/non-surgical management than evidence on the use of iFuse compared with open surgery. The description of conservative/non-surgical management differs between studies but is broadly representative of the stepped pathway including treatments such as, steroid injection, radiofrequency ablation, pain medication, physiotherapy and cognitive behaviour therapy.

The clinical evidence showed that iFuse improved pain, Oswestry disability index (ODI) and health-related quality of life. These improvements were

higher in people receiving treatment with iFuse than those receiving conservative/non-surgical management. One retrospective comparative study recorded lower revision rates after placement of iFuse implants compared with open surgery using screws.

The EAC stated that the included evidence was in the correct patient population including 1 study in people requiring revision surgery following SIJ fusion and 1 study was a sub-group analysis of SIJ pain dysfunction in women with postpartum girdle pain. The 2 RCTs enrolled enough people (over 100) to provide comparisons between treatment arms. One RCT followed up patients for 24 months and 1 retrospective comparative study presented results with up to 6 years follow-up. Nine studies were conducted in the US and 4 in Europe, no studies were conducted within the NHS only. None of the studies were blinded as blinding was not possible due to the surgical nature of SIJ fusion. Nine of the included studies were sponsored by the company and at least 1 author was a company employee.

Table 3: Key studies

Study and design	Participants/ population	Intervention & comparator	Outcome measures and follow up	Results	Withdrawals	Funding	Comments
Dengler et al. (2017b) RCT	103 adults with lower back pain originating from SIJ. All were attending specilaist spine clinics. iFuse: mean age (years) 49.4 (range 27–70), 38 females (73.1%). CM: mean age (years) 46.7 (range 23–69), 37 females (72.5%).	52 people received SIJ fusion with iFuse 51 people received CM (medical therapy and physiotherapy)	12 months follow-up LBP VAS ODI SIJ function (via ASLR) EQ-5D TTO EQ-5D VAS Zung depression scale Patient satisfaction Adverse events	Mean (SD) improvement in LBP VAS at 12 months was 41.6 (±27) for iFuse and 14 (±33.4) for CM (p<0.0001). Mean ODI significantly lower for iFuse (32.1) than CM (36.9) at 12 months (p<0.0001). SIJ function improvement at 6 months was 2 (p<0.0001) for iFuse and 0.2 for CM (p=0.3247). Mean EQ-5D TTO was significantly higher for iFuse (0.74) than CM (0.54) at 12 months (p=0.0009). Mean EQ-5D VAS was significantly lower for iFuse than CM at 12 months (p=0.0005). Mean Zung depression scale was significantly lower for	6 people (2 iFuse, 4 CM) withdrew prior to receiving any intervention. 5 people withdrew during trial (2 iFuse during 6–12 months, 2 CM during 1–3 months and 1 CM during 6–12 months).	Company funded – 1 author is an employee of SI-Bone, 4 authors are paid consultants to SI-Bone.	People in the CM group were permitted to “cross-over” to iFuse after 6 months. 21/49 (43%) people receiving CM crossed over to iFuse at 6 months. Last-observation carried forward was used to estimate CM values at 12 months.

				iFuse (39.6) than CM (44.4) at 12 months (p=0.0035). The same number of adverse events were recorded in both arms.			
Polly et al. (2016a) RCT	148 people with chronic SIJ dysfunction. iFuse: mean age (years) 50.2 (range 25.6–71.7), 75 females (73.5%). NSM: mean age (years) 53.8 (range 29.5–71.1), 28 females (60.9%).	102 people received SIJ fusion with iFuse 46 people received non-surgical management (stepwise medical therapy, physiotherapy, intraarticular SIJ steroid injections and RFA of lateral branches of the sacral nerve roots)	24 months follow-up SIJ VAS ODI EQ-5D TTO SF-36 PCS Adverse events	Mean improvement in SIJ VAS at 24 months was 55.4 for iFuse and 12.2 for NSM after 6 months (p<0.0001). Mean ODI decrease was 28.4 for iFuse (24 months) and 4.6 for NSM (6 months) (p<0.0001). EQ-5D TTO improved by 0.28 (p<0.0001) in the iFuse group (24 months) and 0.06 (p=0.1740) for NSM (6 months). SF-36 PCS improved by 11.2 (p<0.0001) in the iFuse group (24 months) and 3.9 (p=0.2990) for NSM (6 months). iFuse was associated with a higher number of adverse	10 people (7 iFuse, 3 NSM) withdrew prior to receiving any intervention. 15 people withdrew during trial (2 NSM during 1–3 months, 1 iFuse during 3–6 months, 1 iFuse during 6–12 months, 2 iFuse during 12–18 months and 9 iFuse	Company funded – 2 authors are employees of SI-Bone and 2 are paid consultants to SI-Bone.	People in the NSM group were permitted to “cross-over” to iFuse after 6 months. 39/46 (84.8%) people receiving NSM crossed over to iFuse at 6 months. This means that the number of people in each arm changes during the data collected 12–24 months into the study. The EAC stated that these results should be treated with caution.

				events and 3 people required revision surgery.	during 18–24 months.		
Abbreviations used: ASLR – active straight leg raise test; CM – conservative management; LBP – lower back pain; NSM – non-surgical management; ODI – Oswestry disability index; PCS – physical component summary; RCT – randomised controlled trial; RFA – radiofrequency ablation; SIJ – sacroiliac joint; TTO – time trade-off, VAS – visual analogue scale;							

4.2 Summary of economic evidence

The company identified 5 economic studies regarding iFuse. The company stated that it did not think these studies were relevant to the decision problem. The EAC agreed with this as the studies were from a societal perspective (1), regarding diagnosis of SIJ pain (1), or from a US payer perspective (3).

De novo analysis

The company presented two economic models comparing iFuse with open surgery in one and with the stepped pathway in the other.

The model structure for iFuse versus open surgery is simple although clinical experts advised the EAC that open surgery is not widely used in the NHS.

The stepped pathway describes stepwise non-surgical treatments for SIJ pain. This includes medication for chronic pain states (opioids); steroid injections and recurrent steroid injections, and radiofrequency ablation (RFA) and recurrent RFA. The EAC stated that this is a reasonable representation of non-surgical treatments but stated that variations may occur in local practice.

Model parameters

The company used a 7-year time horizon in its model and there was no death state or adjustment for age. The EAC stated that this was appropriate as follow-up data are very limited beyond 4 years and age adjustment for people with a mean age of 50 (mean age in clinical trials) is likely to be minimal.

The EAC made corrections and alterations to the economic model resulting in a small increase in costs for the stepped pathway, a small decrease in the cost of open surgery and no change to the cost of SIJ fixation with iFuse. The changes made by the EAC are listed in the table below. For more information on these changes please see table 11 in the assessment report.

Table 4: EAC changes to model parameters

Variable	Company value	EAC value	EAC source and comments
Length of stay for open surgery (anterior)	8 days	6.7 days	The EAC calculated a weighted average length of stay from two papers by Nystrom et al. (2017) and Ledonio et al. (2014a).
Length of stay for open surgery (posterior)	5.1 days	4 days	The EAC calculated a weighted length of stay based on data from 5 studies.
Length of stay for iFuse	1.7	0.8	The EAC calculated a weighted length of stay based on data from 5 studies.
Procedure time for open surgery (anterior)	104 minutes	110.9 minutes	The EAC calculated a weighted mean procedure time from Nystrom et al. (2017) and Ledonio et al. (2014a).
HRG codes used for open surgery and iFuse (cost of bed day)	Open surgery: £380.99 iFuse: £272.32	Open surgery: £272.32 iFuse: £380.99	NHS reference costs for 2015/2016. The EAC corrected the cost of a bed day for open surgery and iFuse in the model.
Cost of steroid injections	£637	£500	NHS reference costs for 2015/2016. The EAC used the HC29B HRG code only.
Low cost drug regimen	£63.25	£27.38	The EAC found lower costs for the drugs listed by the company in the December 2017 BNF/drug tariff.
High cost drug regimen	£692.98	£669.78	The EAC found lower costs for the drugs listed by the company in the December 2017 BNF/drug tariff.

Variable	Company value	EAC value	EAC source and comments
Good response to treatment (%): iFuse	84%	79.9%	The EAC obtained a figure for success rate from a study by Duhon et al. (2016) at 12 months post-procedure. It felt this was a more accurate estimate as the value used by the company was from a review that reported patient satisfaction.
Good response to treatment (%): open surgery	54%	48%	The EAC replaced the figure for success rate using a value from a study by Kibsgard et al. (2013). The value used by the company was obtained using multiple methods that the EAC did not find appropriate.
Procedure time: open, posterior	104 minutes	110.9 minutes	The EAC calculated a weighted average procedure time from the papers by Nystrom et al. (2017) and Ledonio et al. (2014a).

Costs and resource use

The EAC stated that the costs used by the company for iFuse are consistent with the list price provided by the manufacturer and a clinical expert stated that the listed consumables used with iFuse seem correct. HRG code HN13A-F Major hip procedures was identified as appropriate for the iFuse procedure.

The company also provided costs on the open surgery procedure. HRG codes HC53, 54, 60, 61,62,63,64 Spinal procedures were identified as appropriate for the open surgery procedure. The EAC were unable to find any published information to clarify these costs and therefore sought expert clarification. One

clinical expert noted that cannulated screws would be used for open surgery but could not comment on the exact consumables required without a full description of the open technique used; this was not described in detail by the company. Another clinical expert stated that open surgery would not be carried out very often anymore. However, if it was to be carried out they believe that the posterior SIJ fixation would be the most costly procedure which is in agreement with the company's submission.

In the stepped pathway patients receive a steroid injection, recurrent steroid injections or radiofrequency ablation in a stepped manner. The company identified the correct HRG codes for radiofrequency ablation and the EAC made adjustments to the HRG codes for steroid injection (HC29B day-case inflammatory spinal conditions) and lowered the cost of drugs used.

Results

The EAC made changes to the parameters used in the company's model (as described in table 11 of the assessment report) and corrected 2 errors it identified. The results for the EAC base case are presented in the following table. Please see table 15 of the assessment report for further information on the impact of the individual EAC changes on the company model's results.

Table 5: EAC base case results (table 14 in assessment report)

	iFuse	Open surgery	Stepped pathway
Theatre and hospital costs	£1,309.56	£3,789.17	-
Consumable cost	£4,059.00	£2,260.00	-
Follow-up	£570.90	£570.90	-
Early revision	£25.65	£106.72	-
Training cost	£6.09	-	-
Medication	£1,060.95	£2,627.21	£3,640.82
Late revision	£269.72	£1,111.34	-

Steroid injections	-	-	£3,043.23
RF ablations	-	-	£60.60
Total	**£7,301.87**	**£10,465.34**	**£6,744.65**
Incremental	**-**	**-£3,163.46**	**+£557.22**
Negative values indicate a cost saving			

The EAC base case results show that treatment for SIJ dysfunction with iFuse will lead to cost savings of £3,163.46 per patient in comparison with open surgery but will incur a cost of £557.22 in comparison with the stepped pathway over a 7year time horizon.

The EAC carried out one-way sensitivity analyses to determine the key drivers of the cost model.

For iFuse vs. open surgery, the main driver for cost saving was the bi-annual probability of revision. Other important factors included length of stay for iFuse, % anterior/posterior open surgery procedures, total pain management, unit cost of theatre time and total consumables for iFuse. None of the variations made iFuse cost incurring against open surgery in the one-way sensitivity analysis.

For iFuse vs. the stepped pathway, the main drivers for incurring cost were medication and the number of steroid injection procedures in 6 months. Other important factors included length of stay for iFuse, % good response to steroid injection treatment, unit cost of theatre time and steroid injection procedure costs. The EAC identified a number of factors that could cause significant variation in the cost of iFuse. The EAC noted that the cost of pain medication and steroid injections are highly variable due to the differing levels of pain relief required by individual people. The EAC stated that if a person received more frequent steroid injections, iFuse would become cost saving. The EAC also noted that varying length of stay for iFuse could lead to cost savings for iFuse and highlighted a study that recorded length of stay for iFuse as 0 days

(Duhon et al. 2016), likely indicating that the person receiving the implants had been discharged on the same day as the procedure. The EAC calculated that iFuse would become cost saving (by £494.57 per patient) in comparison to the stepped pathway if the time horizon of the model were extended from 7 to 9 years.

5 Ongoing research

The EAC noted a lack of evidence comparing iFuse to open surgery. However, further research in this area is unlikely either to be carried out, or of likely to be of benefit to the NHS, as clinical experts have advised that open surgery is not routine practice. The EAC did not find any ongoing studies involving iFuse.

6 Issues for consideration by the Committee

Clinical evidence

The clinical evidence includes 2 RCTs and 2 comparative studies. These report significant improvements in pain scores and quality of life (ODI and EQ-5D) in comparison with conservative and non-surgical comparators. No evidence for time until return to work or normal activities following the iFuse procedure was identified.

No evidence was identified that directly compared iFuse with open surgery. Clinical expert advice suggests that open surgery is rarely used to treat SIJ dysfunction in the NHS.

Cost evidence

No published economic studies relevant to the NHS or the decision problem were identified.

Two comparators were included in the modelling, open surgery and the stepped pathway. Clinical expert advice suggests that the stepped pathway is the most appropriate comparator as open surgery is rarely done.

In the EAC base case results iFuse incurs a cost of £557.22 per patient in comparison to the stepped pathway. Upfront costs for iFuse are high but may result in relatively low annual costs whilst the stepped pathway has a moderate annual cost that remains relatively constant over time. If the time horizon of the model was extended from 7 to 9 years iFuse would lead to cost savings of £494.57 per patient and cost saving continues to increase as the time horizon is extended.

The main drivers for cost of iFuse in comparison to the stepped pathway were the cost of pain management and steroid injections and length of stay. The EAC noted that these factors are likely to vary across the patient population.

7 Authors

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Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Evans J, Dale M, Carolan-Rees G et al. iFuse implant system for treating chronic sacroiliac joint pain (February 2018)

B Submissions from the following sponsors:

- SI-Bone

C Related NICE guidance

- NICE clinical guideline Low back pain and sciatica in over 16s: assessment and management
- NICE interventional procedure guidance Minimally invasive sacroiliac joint fusion surgery for chronic sacroiliac pain

D References

Please see EAC assessment report for full list of references.

Appendix B: Comments from professional bodies

Expert advice was sought during topic selection from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society. Please see the collated expert advice table included in the pack for full details.

Mr Mark Thomas

Consultant orthopaedic and spinal surgeon, Frimley Health NHS Foundation Trust

Mrs Elaine Buchanan

Spinal consultant physiotherapist, Oxford University NHS Foundation Trust

Mr Robert Lee

Consultant orthopaedic and spinal surgeon, Royal National Orthopaedic Hospital NHS Trust

Mr David Chapple

Trauma and orthopaedic surgeon, Salisbury NHS Trust

Mr Hilali Noordeen

Consultant spinal surgeon, Royal National Orthopaedic Hospital NHS Trust

Mr Bronek Boszczyk

Consultant spinal surgeon and head of service, University of Nottingham

Appendix C: Comments from patient organisations

Advice and information was sought during topic selection from patient and carer organisations. The following patient and carer organisations responded:

- Action on Pain
- Back Care
- Fighting Back
- Pain Concern
- Pain Relief Foundation
- Pelvic Partnership

Please see the patient expert statements included in the pack for full details.

Appendix D: Decision problem from scope

	Scope issued by NICE
Population	People with unresolved sacroiliac joint dysfunction
Intervention	iFuse implant system
Comparator(s)	open sacroiliac joint fusion surgery using screw or cage systems non-surgical or conservative management, including: • optimisation of medical therapy, • individualised psychological and physical therapy with provision of adequate information and reassurance • steroid injections • sacroiliac joint denervation
Outcomes	The outcome measures to consider include: **Patient outcomes** • back/sacroiliac joint pain relief (including medicine use and post-operative pain scores); • improvement in function and disability from back pain (measured using Oswestry disability index (ODI) or other valid disability scale); • blood loss during surgery; • patient satisfaction; • patient health-related quality of life; • radiographic evidence of union and absence of loosening (x-ray or CT scan to measure bone growth across the fused joint); • time to return to work/normal activities; • peri-operative morbidity and device-related adverse events; • postoperative infection or complications; • reoperation rates. **System outcomes** • procedure time and resources • length of hospital stay.
Cost analysis	Comparator(s): Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters.
Subgroups to be considered	• women of reproductive age • number of implants inserted • unilateral versus bilateral sacroiliac joint implants • previous lumbar surgery
Special considerations, including those	People with chronic sacroiliac pain or lower back pain lasting more than one year may be considered disabled under the Equality Act 2010, if the condition has a substantial and long-term negative effect

related to equality	on their ability to do normal daily activities. Women may experience SIJ dysfunction due to the mechanism of childbirth.	
Special considerations, specifically related to equality issues	The sacroiliac joint and its free movement is critical to normal, vaginal delivery in childbirth. Women of reproductive age having SIJ implants would require caesarean section deliveries after iFuse implant insertion. Most people having surgical interventions for SIJ pain are female but over usual reproductive age.	
	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristics?	Yes
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure MTAC will have relevant information to consider equality issues when developing guidance?	No