

**Evidence for ultrasound-guided knee joint injections**  
(Version 31-1: 13/03//2023)

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**Summary:**

Joint injections can be guided by surface anatomy or ultrasound. The evidence is clear that ultrasound guidance improves injection accuracy in the target intra-articular joint space of large joints, including the knee. However, the clinical significance or impact on longer-term outcomes needs to be clarified, and there needs to be guidance to recommend their use.

The use of the technology is unproven as it has yet to meet the standards of evidence set for efficacy. However, joint injections are done for both diagnostic and therapeutic indications. For diagnostic indications, there are no current AXA levels of evidence guidance. There are also no identifiable harms to using ultrasound at the time of joint injections.

There is, therefore, no specific reason not to recommend the practice, and its use should thus be left up to the individual practitioner's preference. The lack of clinical and cost-effectiveness means image-guided joint injection should be funded at the same cost as a surface anatomy joint injection treatment that delivers a similar diagnostic or therapeutic outcome.

However, NHS Clinical Care Pathways care pathways identify selected patients where image guidance could be appropriate and deemed fundable. These include a history of severe trauma that would derange the joint's normal architecture, failure to identify landmarks due to morbid obesity (BMI>40), or another disease process. Future research should show clinical and cost-effectiveness to alter this guidance.

Technology	Rating	Summary conclusion
AXA 31: Evidence for ultrasound-guided knee joint injections	Green	Image-guided joint injection is recommended based on practitioner preference and funded at the same cost as a surface anatomy joint injection treatment. Image-guided joint injection is recommended and deemed fundable at additional costs for those with a history of severe trauma which would derange the normal architecture of the joint; or if there is a failure to identify landmarks due to morbid obesity (BMI>40) or another disease.

## Background

Joint injections can be undertaken guided by surface anatomy or by ultrasound. The use of ultrasound guidance has been advocated as a technically superior method for performing intra-articular injections, improving injection accuracy in the target intra-articular joint space of large joints, including the knee. <sup>1</sup> The Indications for knee joint injections can be diagnostic or therapeutic (see Cardone et al. <sup>2</sup>) and include

### **Osteoarthritis.**

For the management of Osteoarthritis, NICE guideline [[NG226](#)] <sup>3</sup> recommends intra-articular corticosteroid injections when other pharmacological treatments are ineffective or unsuitable or to support the therapeutic exercise. These injections only provide short-term relief (2 to 10 weeks). NICE also recommends not offering intra-articular hyaluronan injections to manage osteoarthritis.

### **Suspected Septic bursitis (NICE [CKS](#)) <sup>4</sup>**

Aspirate bursal fluid using an aseptic technique and treat empirically with an oral antibiotic which covers staphylococcal and streptococcal species (for an initial period of 7 days) until culture results are known. If swelling, tenderness, and erythema recur, consider repeating aspiration. The period between aspirations should be guided by clinical response.

### **Gout (NICE [CKS](#)) <sup>5</sup> and Gout: diagnosis and management NICE guideline [[NG219](#)] <sup>6</sup>**

If the diagnosis remains uncertain or unconfirmed, arrange investigations in secondary care: Joint aspiration and microscopy of synovial fluid.

If joint aspiration cannot be carried out or the diagnosis remains uncertain, imaging of the affected joint with X-ray, ultrasound, or dual-energy CT may be necessary.

### **Rheumatoid Arthritis ([NICE CKS](#)) <sup>7</sup>**

Seek specialist advice about management. Offer short-term treatment with glucocorticoids, either:

An intra-articular glucocorticoid injection (for example, methylprednisolone acetate or triamcinolone acetonide) for a localised RA flare, if the expertise is available in primary care. The dose depends on the joint's size and the condition's severity.

### **Injection Compounds**

The most common type of intra-articular knee injection compounds are corticosteroids, but other drugs have been used, including infliximab, <sup>8</sup> hyaluronic acid, <sup>9</sup> botulinum toxin, <sup>10</sup> and platelet-rich plasma. <sup>11</sup> Sometimes injections are used in combination; e.g., corticosteroid type and a local anaesthetic such as lidocaine. **The BNF states** Corticosteroid injections also include [Triamcinolone hexacetonide](#) injection, which has various trade names, <sup>12</sup> which is preferred because it is almost insoluble and has a long-acting (depot) effect. Although the BNF reports, its use is [unlicensed](#).

[Triamcinolone acetonide](#) and [methylprednisolone](#) may also be considered for intra-articular injection into larger joints, whilst [hydrocortisone](#) acetate should be reserved for smaller joints or soft-tissue injections. Sometimes injections are used in combination; e.g., corticosteroid type and a local anaesthetic such as lidocaine. <sup>13</sup>

## **Methods**

AXA Health's approach involves learning, adapting, and improving care using high-quality, evidence-based strategies. To achieve this, AXA developed a traffic light system to assess the evidence for developing treatments to identify which treatments are safe and effective. A combination of evidence from NICE guidance, Systematic Reviews, and Randomised Controlled Trials generates traffic light ratings.

The following definitions are used in the traffic light system:

Green: Conventional Treatments\* that have met the standards of evidence we've set for safety and efficacy.

Amber: Unproven Treatments that have met the standards of evidence we've set for safety but not efficacy.

Red: Unproven Treatments\* that have not met the standards of evidence we've set for safety.

## **Search Strategy**

The following databases were searched: the Trip Database ([www.tripdatabase.com](http://www.tripdatabase.com)) - which searches the primary higher-level evidence sources, e.g., NICE, AHRQ, Cochrane etc.; PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) - covers the leading journal articles and Google - used for general searching and to look for specific documents from the FDA, Aetna, NHS etc.

## **Analysis**

Each piece of evidence retrieved is subjected to an assessment of its quality and the overall effect. Based on this evidence, an overall conclusion is reached, and a traffic light rating is awarded where appropriate. This evidence is then shared with key stakeholders for critical feedback.

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## **Results of the Evidence Review**

**2022** NICE [Osteoarthritis: assessment and management \(update\)](#)

### **Evidence reviews for the clinical and cost-effectiveness of intra-articular injections for the management of osteoarthritis**

Intra-articular stem cell therapy (image-guided) compared to placebo included two ultrasound knee joint injection RCTs

Kuah D, et al. Safety, tolerability and 28 efficacy of intra-articular Progenza in knee osteoarthritis: a randomised double-blind placebo<sup>29</sup> controlled single ascending dose study. *Journal of Translational Medicine*. 2018; 16(1):49

**Popn:** Knee osteoarthritis Mean age (SD): 53.3 (7.6) years (n=20)

Kellgren Lawrence grade 1-3 knee osteoarthritis with moderate-severe pain in the study knee Severity: Kellgren Lawrence grades 1-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/unclear

**Intervention:** Intra-articular stem cell therapy (image-guided) (n=16)

Expanded allogeneic mesenchymal stem cells from human adipose tissue (Progenza) 3.9 million and 6.7 million cells (combined groups) given as one injection.

Concomitant therapy: No additional information

**Outcomes:** Pain at >3 months Serious adverse events at >3 months

There was a statistically significant within-group improvement in VAS pain scores from baseline at all time points for the PRG combined group, with highly significant improvements seen at months 3, 6, 9 and 12 ( $p \leq 0.005$ ) while VAS pain scores in the placebo group showed marginal improvement.

**Conclusion:** When administered as a single intra-articular injection to patients with symptomatic knee OA, PRG was safe and well tolerated.

Lee WS et al. Intra-articular injection of autologous adipose tissue<sup>31</sup> derived mesenchymal stem cells for treating knee osteoarthritis: A phase iib, 32 randomised, placebo-controlled clinical trial. *Stem Cells Translational Medicine*. 2019; 33 8(6):504-511

**Popn:** Mean age (SD): 62.7 (5.5) years N = 24 Definition: Osteoarthritis of the knee joint (Kellgren-Lawrence grade 2-4) Severity: Majority Kellgren Lawrence grade 2-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/unclear

**Intervention:** Intra-articular stem cell therapy (image-guided) (n=12) 3mL adipose-derived mesenchymal stem cells ( $1 \times 10^8$  cells) given in 1 injection Placebo (n=12) 3mL of saline given in 1 injection Concomitant therapy: The rescue analgesic was paracetamol at 4000 mg or less per day. Other analgesics were not permitted, and any medications were recorded.

**Outcomes:** Serious adverse events at >3 months

**Conclusion:** An intra-articular injection of autologous AD-MSCs provided satisfactory functional improvement and pain relief for patients with knee osteoarthritis in the outpatient setting without causing adverse events at six months follow-up. A larger sample size and long-term follow-up are required. *Stem Cells Translational Medicine* 2019;8:504-511.

## 2021 European Society of Musculoskeletal Radiology (ESSR)

[Clinical indications for image-guided interventional procedures in the musculoskeletal system: a Delphi-based consensus paper from the European Society of Musculoskeletal Radiology \(ESSR\)—part V, knee.](#)

This is more a guideline that makes ten recommendations, including “*Intra-articular US-guided procedures around the knee joint, such as arthrocentesis and intra-articular injections, are more accurate than palpation-guided procedures, resulting in improved fluid aspiration and injection therapeutic outcome(s).*”

## **NHS guidance**

There is evidence of [NHS referral advice](#) as part of the NHS Clinical Care Pathways guidance to secondary care services for ultrasound-guided corticosteroid injections for the knee.

The guidance does not apply to patients under 18 years old, patients having treatment for managing pain due to cancer or patients with inflammatory arthritides (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis).

Referral to secondary care services for ultrasound-guided corticosteroid injections for the named joints in box one will only be funded by CCGs when at least one of the criteria has been met and thoroughly documented:

- History of severe trauma which would derange the normal architecture of the joint.
- Failure to identify landmarks due to morbid obesity (BMI>40) or another disease process.
- Failure of the initial attempt of a corticosteroid injection due to inability to identify landmarks.
- No symptomatic relief after two blind injections.
- Significant adverse effects associated with a landmark-guided injection, such as severe procedural pain.

AND

- No response over six months to conservative treatment.
- Patients referred to secondary care due to diagnostic uncertainty and advised to have a corticosteroid injection should not be referred for an ultrasound-guided injection in secondary care (unless the above criteria are met).
- In cases where the above criteria were met the CCG would fund up to 2 joint injections.

There is evidence that this guidance has been taken up and used by an NHS Integrated Care Board commission image-guided joint injections. <sup>14</sup>

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## **Systematic reviews**

**2021** [Ultrasound-Guided Knee Injections Are More Accurate Than Blind Injections: A Systematic Review of Randomized Controlled Trials.](#)

This review included 12 studies covering 1431 patients and 1315 knees. Seven of the studies did a direct comparison between ultrasound-guided and blind knee injections.

- **Ultrasound-guided injections were more accurate** compared with blinded knee injections in every study.

**Effusion of unknown origin or suspected infection** (only diagnostic)

**2016** [Ultrasound-guided versus landmark in knee arthrocentesis: A systematic review.](#) The review included 9 controlled studies covering 715 adult patients and 725 knee joints.

A systematic review of the literature was performed until August 2015. All controlled trials reporting the accuracy or clinical efficacy between USG and LM knee joint arthrocentesis were selected.

- There was a statistically significant difference in favour of USG for knee arthrocentesis accuracy rate (risk ratio 1.21; 95% CI: 1.13–1.29)
- lower procedural pain scores (WMD 2.24; 95% CI: 2.92 to 1.56)
- more aspiration volume (WMD 17.06; 95% CI: 5.98–28.13;
- and decreased pain score 2 weeks after injection (WMD 0.84; 95% CI: 0.42–1.27)

**Conclusions: Ultrasound-guided knee joint arthrocentesis offer a significantly greater accuracy** and clinical improvement over landmark technique in adults with knee pain or joint effusion

**2013** [Where and how to inject the knee--a systematic review.](#)

This systematic review included 23 studies in determining the accuracy of intra-articular knee injection (IAKI), whether this varied by site, use of image-guidance, and experience of injectors, and whether the accuracy of injection, site or use of image-guidance influenced outcomes following IAKIs.

- Within-study analyses suggested IAKIs at the superomedial patellar, medial mid patellar (MMP), superolateral patellar (SLP), and lateral suprapatellar bursa sites were more accurate when using image guidance than when blinded
- Pooling data across studies suggested blinded IAKIs at the SLP site were most accurate (87%) while MMP (64%) and anterolateral joint line (ALJL) sites were (70%) least accurate.
- Overall, about one in five blinded IAKIs were inaccurate.
- There was some evidence that the injector's experience was linked with improved accuracy for blinded though not image-guided, injections.

The review concluded that **Image-guided IAKIs are modestly more accurate than blinded intra-articular knee injections**, especially at the MMP and ALJL sites.

2011 [The most accurate approach for intra-articular needle placement in the knee joint: a systematic review](#)

Nine studies were included.

- The superolateral approach was investigated most, resulting in the highest pooled accuracy rate of 91% (95% CI 84-99%).
- Guidance of intra-articular needle placements by imaging techniques may enhance the accuracy.
- The costs and extra time associated with these techniques should be considered.

## References

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