NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Autologous chondrocyte implantation using 3D collagen matrix (novocart 3D) for treating articular cartilage defects of the knee

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of 3D collagen matrix (novocart 3D) within its marketing authorisation for treating articular cartilage defects of the knee.

Background

Articular cartilage is hyaline cartilage on the joint surfaces of the bone. Articular cartilage defects can be caused by injury (often sports related), or arthritis, or it can occur spontaneously. Cartilage damage may also arise because of instability or abnormal unbalanced pressures in the joint. Damage of the articular cartilage does not heal on its own and can cause symptoms such as pain, swelling, locking and giving way of the joint. In addition, damage to the cartilage and surrounding tissues can cause osteoarthritis and lead to a need for partial or total joint replacement surgery in later life. Cartilage damage can be described by size (area) and graded by depth. Commonly used scoring systems include the international cartilage repair society (ICRS) grading system, and the Outerbridge system.

There are no reliable estimates of the prevalence of symptomatic articular cartilage defects, although it is estimated that around 10,000 people need treatment for cartilage damage every year in the UK.

The aim of treatment is to relieve symptoms such as locking, swelling, and instability, and to improve general mobility. Treatment options include debridement (removal of damaged cartilage), re-establishing the articular surface (microfracture, mosaicplasty and autologous chondrocyte implantation), osteotomy, and joint replacement. Osteotomy and joint replacement are options reserved for larger lesions and those where cartilage repair has failed.

In autologous chondrocyte implantation, healthy chondrocytes are harvested arthroscopically from the affected joint. The cells are cultured in a laboratory and then implanted into the damaged areas of the cartilage. The method for delivering the cells to the damaged area has evolved over time.

NICE technology appraisal guidance 477 recommends traditional autologous chondrocyte implantation (at the OsCell John Charnley Laboratory) with either the use of a periosteal or collagen membrane as an option for treating symptomatic articular cartilage defects of the knee (Oswestry Risk of Knee Arthroplasty score is 3 or 4), only if:

- the person has not had previous surgery to repair articular cartilage defects

- there is minimal osteoarthritic damage to the knee (as assessed by clinicians experienced in investigating knee cartilage damage using a validated measure for knee osteoarthritis)
- the defect is over 2 cm^2 and
- the procedure is done at a tertiary referral centre.

NICE technology appraisal guidance 508 recommends autologous chondrocyte implantation as an option for treating symptomatic articular cartilage defects of the knee, only if:

- the person has not had previous surgery to repair articular cartilage defects,
- there is minimal osteoarthritic damage to the knee and
- the defect is over $2cm^2$.

The technology

Autologous chondrocyte implantation is a technique where cartilage is developed in vitro. (Novocart, TETEC AG) is a procedure where chondrocytes cultured from the patient's own cells which are seeded onto a bioresorbable three-dimensional collagen scaffold is a and secured directly into the area of cartilage defect.

Autologous chondrocyte implantation using novocart does not currently have a marketing authorisation in the UK for people with articular cartilage defects. It has been studied in randomised phase III clinical trials compared with microfracture in people with articular cartilage defects of the knee.

Intervention(s)	Autologous chondrocyte implantation using 3D collagen matrix (novocart)
Population(s)	People with articular cartilage defects of the knee.
Comparators	For defects up to $2cm^2$: • Microfracture (marrow stimulation) For defects over $2cm^2$: • Autologous chondrocyte implantation (ACI) with or without novocart As appropriate for lesion size: • Mosaicplasty • Best supportive care (non-operative intervention including exercise, weight loss, analgesia, corticosteroid injections, transcutaneous electrical nerve stimulation, heat/cold, crutches)

Outcomes	The outcome measures to be considered include: • pain • joint function including long-term function • rates of retreatment • activity levels • avoidance of osteoarthritis including joint replacement • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If evidence allows, subgroup analyses by lesion size will be considered. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. If the evidence allows consideration will be given to subgroups stratified by duration of symptoms, size and site of lesion, previous exposure to surgical treatment, and for cartilage defects secondary to malalignment.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Autologous chondrocyte implantation for treating symptomatic articular cartilage defects of the knee (2017). NICE Technology Appraisal 477. Review date 2020. Autologous chondrocyte implantation using chondrosphere for treating symptomatic articular cartilage defects of the knee (2018). NICE Technology Appraisal 508. Review date 2021.

	Related Interventional Procedures: Microstructural scaffold (patch) insertion without autologous cell implantation for repairing symptomatic chondral knee defects (2016). NICE interventional procedures guidance 560. Mosaicplasty for symptomatic articular cartilage defects of the knee (2018). NICE interventional procedures guidance 607. Related NICE Pathways: Musculoskeletal conditions (2019) NICE pathway https://pathways.nice.org.uk/pathways/
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) section 13 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for autologous chondrocyte implantation using 3D collagen matrix been included in the scope?

Do the relevant comparators depend on the size of the cartilage lesion?

Is microfracture used for lesions over 2cm^2 in clinical practice?

Is mosaicplasty used in current practice? Is mosaicplasty a relevant comparator for novocart?

Is novocart intended for primary ACI repair (in people who have not had previous surgery to repair articular cartilage) and secondary repair (in people who have had previous surgery (e.g. microfracture)?

Will patients' cells be cultured in the UK or in laboratories outside the UK? If novocart was cultured outside of the UK would this pose any barriers to implementation in the NHS?

Which treatments are considered to be established clinical practice in the NHS for articular cartilage defects of the knee?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom autologous chondrocyte implantation using 3D collagen matrix is expected to be more clinically effective and cost effective

or other groups that should be examined separately? Is the size of the defect an appropriate subgroup?

Where do you consider autologous chondrocyte implantation using 3D collagen matrix will fit into the existing NICE pathway, musculoskeletal conditions?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which autologous chondrocyte implantation using 3D collagen matrix will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider autologous chondrocyte implantation using 3D collagen matrix to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of autologous chondrocyte implantation using 3D collagen matrix can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?