NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Multiple Technology Appraisal

Autologous chondrocyte implantation for repairing symptomatic articular cartilage defects of the knee (including a review of TA89)

Draft scope

Draft remit

To appraise the clinical and cost effectiveness of autologous chondrocyte implantation within the applicable licensed indications for repairing symptomatic articular cartilage defects of the knee (to include a review of technology appraisal 89 where appropriate).

Background

Articular cartilage refers to hyaline cartilage on the articular surfaces of the bone. Articular cartilage damage in the knee can be caused directly by acute injury, often as a result of sporting activity, or from repetitive trauma such as high-impact sports. The condition may arise without obvious trauma in individuals with defective cartilage (a condition called osteochondritis dissecans). Damage of the articular cartilage does not heal on its own and can be associated with symptoms such as knee pain, knee swelling, knee locking and giving way of the knee joint. Ultimately, mechanical damage to the joint surface can lead to osteoarthritis. The International Cartilage Repair Society has a grading system by which cartilage defects can be ranked (grade 0-IV), where grade III indicates lesions having deep crevices in more than 50% of the cartilage layer, and grade IV is where the cartilage tear exposes the underlying bone.

There are no reliable estimates of the prevalence of symptomatic articular cartilage defects of the knee, although it is estimated that every year in the UK, around 10,000 people have cartilage damage serious enough to require treatment. The number of people with symptomatic cartilage defects suitable for autologous chondrocyte implantation is estimated to be between 200 and 500 people per year in the UK.

Current treatment options include symptomatic relief, knee lavage with or without debridement (removal of damaged cartilage) and procedures to re-establish the articular surface. Interventions that aim to re-establish the articular surface include marrow stimulation techniques (such as microfracture), mosaicplasty (also known as osteochondral transplantation) and implantation of healthy cartilage cells (chondrocytes), a technique known as autologous chondrocyte implantation. For larger lesions, osteotomy (realigning of the knee), knee replacement and best supportive care would be the main options.

NICE technology appraisal 89 does not recommend autologous chondrocyte implantation for the treatment of articular cartilage defects of the knee except

in the context of ongoing or new clinical studies. NICE guidance recommends that mosaicplasty (NICE Interventional Procedure Guidance 162) should only be used with special arrangements for clinical governance, consent and audit or research.

The technologies

Autologous chondrocyte implantation (ACI) comprises a series of procedures. First chondrocytes are harvested arthroscopically from the affected knee joint. The cells are cultured in a laboratory for a few weeks and in a second surgical procedure, the cells are implanted into the damaged areas of the cartilage.

- ChondroCelect (TiGenix) is used as part of an ACI procedure. The combination of ChondroCelect (the product) and ACI (the procedure) is called Characterised Chondrocyte Implantation. The active substance in ChondroCelect is the patient's own cartilage cells. A biopsy (a small sample) is taken from the patient's cartilage in the knee in an arthroscopy. The cartilage cells (chondrocytes) are then characterised and those which are identified as capable of producing hyaline cartilage are grown and expanded in the laboratory to provide enough cells to make up a suspension that can be used to treat the cartilage defect. Open knee surgery is performed in which cells are either injected under a biodegradable cover sutured over the cartilage defect, or the cells are applied directly onto a biodegradable membrane which then is sutured over the cartilage defect ('cell seeding' technique).

  ChondroCelect has a UK marketing authorisation for the "repair of single symptomatic cartilage defects of the femoral condyle of the knee (International Cartilage Repair Society [ICRS] grade III or IV) in adults". The randomised controlled trial that supported the marketing authorisation for Chondrocelect included patients with lesions between 1-5cm².

- Matrix-applied autologous cultured chondrocytes (MACI, Sanofi) is used as part of an ACI procedure. MACI is an implant consisting of a porcine derived collagen membrane which contains a patients' own cartilage cells that have been taken from the knee and grown outside the body (autologous chondrocytes). MACI has a marketing authorisation for "the repair of symptomatic, full-thickness cartilage defects of the knee (grade III and IV of the Modified Outerbridge Scale) of 3-20 cm^2 in skeletally mature adult patients."

- 'Traditional' ACI can be carried out without the branded products above under hospital exemptions from the 'advanced therapy medicinal products' regulation.

Intervention(s)	• Characterised Chondrocyte Implantation using ChondroCelect • Matrix-applied characterised autologous cultured chondrocytes (MACI) • Traditional autologous chondrocyte implantation (currently authorised on hospital exemptions from the 'advanced therapy medicinal products' regulation)
Population(s)	Adults with a single symptomatic defect in the cartilage of the femoral condyle of the knee with • International Cartilage Repair Society (ICRS) grade III or IV • lesions of more than 1 cm^2 • no advanced osteoarthritis
Comparators	For small lesions: • Microfracture (marrow stimulation) • Mosaicplasty For large lesions: • Osteotomy (realignment of the knee) • Knee replacement • Best supportive care The interventions will be compared with each other where appropriate.
Outcomes	The outcome measures to be considered include: • pain • knee function including long-term function • rates of retreatment • activity levels • avoidance of osteoarthritis including knee 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. 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	Guidance will only be issued in accordance with the marketing authorisation. If the evidence allows consideration will be given to subgroups stratified by duration of symptoms (less or more than 3 years), size of lesion, and previous exposure to surgical treatment.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 89, May 2005, 'Autologous chondrocyte implantation (ACI) for the treatment of cartilage injury (review of Technology Appraisal16). Review Proposal deferred to 2013. Related Interventional Procedures: Interventional Procedure No.162, Mar 2006, 'Mosaicplasty for knee cartilage defects'.

Questions for consultation

Have the most appropriate interventions been included in the scope?

Have the most appropriate comparators treating articular cartilage defects of the knee been included in the scope?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom the technologies are expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 ChondroCelect is 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 the technology 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 the technology 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.