

FEP 7.01.48 Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions

Effective Date: July 15, 2018

Related Policies:

7.01.15 Meniscal Allografts and Other Meniscal Implants
8.01.52 Orthopedic Applications of Stem Cell Therapy
(Including Allograft and Bone Substitute Products Used With Autologous Bone Marrow)

Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions

Description

A variety of procedures are being developed to resurface articular cartilage defects. Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral defect. Second- and third-generation techniques include combinations of autologous chondrocytes, scaffolds, and growth factors.

FDA REGULATORY STATUS

The culturing of chondrocytes is considered by FDA to fall into the category of manipulated autologous structural cells, which are subject to a biologic licensing requirement. In 1997, Carticel® (Genzyme; now Vericel) received FDA approval for the repair of clinically significant, "...symptomatic cartilaginous defects of the femoral condyle (medial lateral or trochlear) caused by acute or repetitive trauma..."

In December 2016, MACI® (Vericel) received FDA approval (Biologics License Application (BLA) 125603) for "the repair of symptomatic, single or multiple full-thickness cartilage defects of the knee with or without bone involvement in adults." MACI® consists of autologous chondrocytes that are cultured onto a bioresorbable porcine-derived collagen membrane. In 2017, production of Carticel® was phased out, and MACI® is the only ACI product available in the United States.

A number of other second-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development or testing or are available outside of the United States. They include Atelocollagen (Koken), a collagen gel; Bioseed® C (BioTissue Technologies), a polymer scaffold; CaReS (Ars Arthro), collagen gel; Cartilix (Biomet), a polymer hydrogel; Chondron (Sewon Cellontech), a fibrin gel; Hyalograft C (Fidia Advanced Polymers), a hyaluronic acid-based scaffold; NeoCart (Histogenics), an ACI with a 3-dimensional chondromatrix in a phase 3 trial; and Novocart®3D (Aesculap Biologics), a collagen-chondroitin sulfate scaffold in a phase 3 trial. ChondroCelect® (TiGenix), characterized as a chondrocyte implantation with a completed phase 3 trial, uses a gene marker profile to determine in vivo cartilage-forming potential and thereby optimizes the phenotype (eg, hyaline cartilage vs fibrocartilage) of the tissue produced with each ACI cell batch. Each batch of chondrocytes is graded based on the quantitative gene expression of a selection of positive and negative markers for hyaline

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cartilage formation. Both Hyalograft C and ChondroCelect® have been withdrawn from the market in Europe.

POLICY STATEMENT

Autologous chondrocyte implantation may be considered **medically necessary** for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma when all of the following criteria are met:

- Adolescent patients should be skeletally mature with documented closure of growth plates (eg, ≥ 15 years). Adult patients should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (eg, < 55 years)
- Focal, full-thickness (grade III or IV) unipolar lesions of the weight-bearing surface of the femoral condyles, trochlea, or patella at least 1.5 cm² in size
- Documented minimal to absent degenerative changes in the surrounding articular cartilage (Outerbridge grade II or less), and normal-appearing hyaline cartilage surrounding the border of the defect
- Normal knee biomechanics or alignment and stability achieved concurrently with autologous chondrocyte implantation.

Autologous chondrocyte implantation for all other joints, including the talar, and any non-FDA approved indications other than those listed above is considered **investigational**.

POLICY GUIDELINES

For smaller lesions (eg, < 4 cm²), if débridement is the only prior surgical treatment, then consideration should be given to marrow-stimulating techniques before autologous chondrocyte implantation (ACI) is performed.

The average defect size reported in the literature is about 5 cm²; many studies treated lesions as large as 15 cm².

Severe obesity (eg, body mass index > 35 kg/m²) may affect outcomes due to the increased stress on weight-bearing surfaces of the joint.

Misalignment and instability of the joint are contraindications. Therefore, additional procedures, such as repair of ligaments or tendons or creation of an osteotomy for realignment of the joint, may be performed at the same time. In addition, meniscal allograft transplantation may be performed in combination, either concurrently or sequentially, with ACI. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

The entire matrix-induced ACI procedure consists of 4 steps: (1) initial arthroscopy and biopsy of normal cartilage, (2) culturing of chondrocytes on an absorbable collagen matrix, (3) a separate arthrotomy to place the implant, and (4) postsurgical rehabilitation. The initial arthroscopy may be scheduled as a diagnostic procedure; as part of this procedure, a cartilage defect may be identified, prompting biopsy of normal cartilage in anticipation of a possible chondrocyte transplant. The biopsied material is then sent for culturing and returned to the hospital when the implantation procedure (ie, arthrotomy) is scheduled.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

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RATIONALE

Summary of Evidence

For individuals who have focal articular cartilage lesion(s) of the weight-bearing surface of the femoral condyles, trochlea, or patella who receive ACI, the evidence includes systematic reviews, randomized controlled trials, and prospective observational studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, and quality of life. There is a large body of evidence on ACI for the treatment of focal articular cartilage lesions of the knee. For large lesions, ACI results in better outcomes than microfracture, particularly in the long term. In addition, there is a limit to the size of lesions that can be treated with osteochondral autograft transfer, due to a limit on the number of osteochondral cores that can be safely harvested. As a result, ACI has become the established treatment for large articular cartilage lesions in the knee. In 2017, first-generation ACI with a collagen cover was phased out and replaced with an ACI preparation that seeds the chondrocytes onto a bioresorbable collagen sponge. Although the implantation procedure for this second-generation ACI is less technically demanding, studies to date have not shown improved outcomes compared with first-generation ACI. Some evidence has suggested an increase in hypertrophy (overgrowth) of the new implant that may exceed that of the collagen membrane covered implant. Long-term studies with a larger number of patients will be needed to determine whether this hypertrophy impacts graft survival. Based on mid-term outcomes that approximate those of first-generation ACI and the lack of alternatives, second-generation ACI may be considered an option for large disabling full-thickness cartilage lesions of the knee. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have focal articular cartilage lesions of joints other than the knee who receive ACI, the evidence includes systematic reviews of case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, and quality of life. The greatest amount of literature is for ACI of the talus. Comparative trials are needed to determine whether ACI improves outcomes for lesions in joints other than the knee. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Academy of Orthopaedic Surgeons

In 2010 guidelines on the diagnosis and treatment of osteochondritis dissecans, the American Academy of Orthopaedic Surgeons did not recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable osteochondritis dissecans lesion.²⁹ This finding of insufficient evidence was based on a systematic review that found 4 level IV studies addressing cartilage repair techniques for an unsalvageable osteochondritis dissecans lesion. Because each level IV articles used different techniques, different outcome measures, and differing lengths of follow-up, the Academy deemed the evidence for any specific technique inconclusive.

National Institute for Health and Care Excellence

In 2017, the National Institute for Health and Care Excellence updated its 2005 guidance on the use of autologous chondrocyte implantation.³⁰ The Institute recommended 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 (as assessed by clinicians experienced in investigating knee cartilage damage using a validated measure for knee osteoarthritis);

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- the defect is over 2 cm²; and,
- the procedure is done at a tertiary referral centre.”

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
September 2013	Update Policy	Policy updated with literature review, references 12 and 39-42 added; sections and statements on minced cartilage moved to policy No. 7.01.48. Policy title change (Osteochondral Autografts and Allografts and "Other Cell-based Treatments" removed from title.
September 2015	Update Policy	Policy updated with literature review; references 5 and 7 added; policy statements unchanged.
June 2017	Update Policy	Clinical input reviewed; references 8 and 32-33 added. Autologous chondrocyte implantation of the patella considered medically necessary; need for a prior surgical procedure removed from policy statement. Policy updated with literature review through March 2, 2017; references 5, 7, 10, 12, and 19 added. Rationale extensively revised to focus on available products. Investigational statement on matrix-induced autologous chondrocyte implantation removed.
March 2018	Update Policy	Policy updated with literature review through November 13, 2017, focusing on matrix-induced autologous chondrocyte implantation of the patella; references 12-18 added. Matrix-induced autologous chondrocyte implantation of the patella is considered medically necessary. In the investigational statement the wording: "and any indications other than

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		those listed above” changed to “and any non-FDA approved indications” for clarification.
June 2018	Update Policy	Policy updated with literature review through February 5, 2018; references 6, 8, 22, 27, and 30 added. Policy statements unchanged.

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