Description of Procedure or Service

Autologous chondrocyte implantation (ACI) or transplantation is a form of tissue engineering that creates a graft from a patient’s own cartilage cells to repair defects in articular cartilage. The procedure involves the collection of cartilage cells, which are grown in a laboratory to create new cartilage tissue. This new tissue is then implanted into the defect, with the goal of improving the quality of cartilage repair.

Background

Hyaline cartilage, the naturally occurring cartilage which covers the weight-bearing surfaces of bones in mobile joints, is very durable but has a low capacity for regeneration because of its avascular and relatively acellular composition. Osteochondral (OC) surfaces that are damaged by trauma or degenerative processes usually fill in with fibrocartilage, which is less suitable for absorbing stress than hyaline cartilage, making the joint susceptible to further damage and development of arthritis.

Nonsurgical treatments for damage to articular cartilage include weight reduction, physical therapy, braces and orthotics, intraarticular injection of hyaluronic acid derivatives, and nonsteroidal anti-inflammatory agents. Many surgical options are available, including cartilage debridement or repair, subchondral drilling, abrasion, spongialization, microfracture, implants, OC grafting, autologous chondrocyte implantation (ACI), and total joint replacement.

There is no standard approach to the treatment of hyaline cartilage defects in the knee. Results from these conventional methods can be suboptimal or short-lasting, except in individuals with very low activity demands. If defects progress to severe osteoarthritis, total knee replacement (TKR) may become necessary.

ACI involves surgical removal of a small piece of articular cartilage, harvesting of cells from the cartilage, growth of these cells in a specialized laboratory, and implanting the cultured cells over the cartilage lesion, with the goal of restoring resilient, durable cartilage at the site of injury. In first-generation ACI, the cultured cells are injected under a periosteal membrane that is usually taken from the tibia of the patient and sutured over the knee lesion. In second- and third-generation ACI, the cultured cells are injected under or grown attached to a synthetic membrane or scaffold that is sutured over or adhered to the knee lesion. ACI was first performed in 1994 in Sweden, at the University of Göteborg (Brittberg et al., 1994) and has been performed on more than 55,000 patients worldwide since its introduction.

Current National Institute for Health and Care Excellence (NICE) guidelines recommend against ACI for the treatment of articular cartilage defects of the knee joint, except in the context of ongoing or new clinical studies that are designed to generate robust and relevant outcomes data, including the
measurement of health-related quality of life and long-term follow-up. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure (NICE, 2005). This guidance was reviewed in 2012 but updating was delayed pending publication of results of certain relevant clinical trials (NICE, 2012). A recent systematic review by the UK National Health Service concluded that, although the evidence base concerning ACI had improved since the last appraisal by NICE, research was still needed to assess the long-term safety and efficacy of new forms of ACI (Mistry et al., 2017).

The SUMMIT (Superiority of Matrix-induced autologous chondrocyte implant versus Microfracture for Treatment of symptomatic articular cartilage defects) trial compared matrix-applied chondrocyte implantation (MACI®) against MF. The TIG/ACT/01/2000 (TIG/ACT) trial compared ACI with characterized chondrocytes against MF. The ACTIVE trial compared several forms of ACI against standard treatments, mainly MF. In the SUMMIT trial, improvements in knee injury and osteoarthritis outcome scores (KOOSs), and the proportion of responders, were greater in the MACI group than in the MF group. In the TIG/ACT trial there was improvement in the KOOS at 60 months, but no difference between ACI and MF overall. Patients with onset of symptoms < 3 years' duration did better with ACI. Results from ACTIVE have not yet been published. Survival analysis suggests that long-term results are better with ACI than with MF. Economic modelling suggested that ACI was cost-effective compared with MF across a range of scenarios.

From the Mistry et al. analysis, the main limitation was the lack of randomized controlled trial data beyond 5 years of follow-up. A second was that the techniques of ACI are evolving, so long-term data come from trials using forms of ACI that are now superseded. In the modelling, they assumed that durability of cartilage repair as seen in studies of older forms of ACI could be applied in modelling of newer forms. A third was that the high list prices of chondrocytes are reduced by confidential discounting. The main research needs are for longer-term follow-up and for trials of the next generation of ACI.

**Regulatory Status**

Implantation of autologous chondrocytes is a surgical procedure and, as such, is not subject to regulation by the FDA. However, the FDA does license biological products such as: Carticel (Vericel Corp., formerly manufactured by Genzyme Biosurgery) and ACI-Maix collagen membrane (Vericel Corp.). Several other products have been considered or tested for the purpose of ACI but have not yet received FDA clearance.

**Benefit Application**

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits.
Policy Statement

GEHA will provide coverage for autologous chondrocyte implantation/transplantation when it is determined to be medically necessary because the medical criteria and guidelines as documented below have been demonstrated.

When Autologous Chondrocyte Transplantation is covered

GEHA considers Autologous Chondrocyte Implantation (ACI) medically necessary for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma and when there are symptoms of disabling knee pain related to a full thickness, focal chondral defect and all of the following criteria are met:

- Body mass index (BMI) less than or equal to 35
- Failure of conservative therapy (minimum of 2 months of physical therapy) as well as established surgical interventions (i.e., microfracture, drilling, abrasion, or osteochondral autograft). Please note: neither diagnostic arthroscopy, lavage, or debridement are considered adequate to meet this criterion; and
- Focal articular cartilage defect down to but not through the subchondral bone on a load bearing surface of the femoral condyle (medial, lateral, trochlear) or the patella); and
- Focal, full-thickness (grade III or IV) unipolar lesions of the patella or the weight bearing surface of the femoral condyles or trochlea 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
- Adolescent patients should be skeletally mature with documented closure of growth plates (e.g., 15 years or older). Adult patients should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., younger than 55 years)

When Autologous Chondrocyte Transplantation is not covered

Autologous chondrocyte transplantation is considered experimental/investigational for all other indications, including but not limited:

- Talar lesions, or lesions of other joints (e.g., hip and shoulder)
- For individuals with a prior total meniscectomy
- Osteochondritis dissecans lesions
- Initial or first line surgery
- Patients with an unstable knee
- Osteoarthritis or other inflammatory disease of the joint (where an osteoarthritic or inflammatory process significantly and adversely affects the quality of the peri-lesional cartilage)
- Kissing lesions
- Previous cancer in the bones, cartilage, fat, or muscle of the treated limb.

The following procedures are considered experimental/investigational and thus, not covered:
- Combined meniscal allograft and autologous chondrocyte implantation of the knee
- Combined autologous chondrocyte implantation and osteochondral autograft transfer system for surgical repair of cartilage defects of the knee

**Policy Guidelines**

This procedure is generally considered contraindicated in individuals with a known history of an allergy to gentamicin and for individuals with sensitivities to materials of bovine origin.

**Physician documentation**

Completed GEHA Osteochondral Procedure form (This can be found on the geha.com website).

Results of Arthroscopic assessment or MRI History and Physical performed with the last 12 months including height and weight

Documentation of conservative treatment and results of conservative treatment

Any other such documentation to provide evidence that member meets the coverage criteria set forth in this policy.

Applicable Codes include but are not limited to:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>27412</td>
<td>Autologous chondrocyte implantation, knee</td>
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<tr>
<td>J7330</td>
<td>Hyaluronan or derivative, Synvisc or Synvisc-One, for intra-articular injection, 1 mg</td>
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<tr>
<td>S2112</td>
<td>Arthroscopy, knee, surgical for harvesting of cartilage (chondrocyte cells)</td>
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**Scientific references**


9. MACI FDA approval: https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/approvedproducts/ucm533177.htm


**Policy implementation and updates**

June 2018 Complete reformatting and updates to policy content; clarification and expansion of covered vs non-covered indications.