Autologous Chondrocyte Implantation to the Knee

**Policy Number:** 2015M0085A  
**Effective Date:** August 01, 2015

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**INSTRUCTIONS:**

“Medical Policy assists in administering UCare benefits when making coverage determinations for members under our health benefit plans. When deciding coverage, all reviewers must first identify enrollee eligibility, federal and state legislation or regulatory guidance regarding benefit mandates, and the member specific Evidence of Coverage (EOC) document must be referenced prior to using the medical policies. In the event of a conflict, the enrollee’s specific benefit document and federal and state legislation and regulatory guidance supersede this Medical Policy. In the absence of benefit mandates or regulatory guidance that govern the service, procedure or treatment, or when the member’s EOC document is silent or not specific, medical policies help to clarify which healthcare services may or may not be covered. This Medical Policy is provided for informational purposes and does not constitute medical advice. In addition to medical policies, UCare also uses tools developed by third parties, such as the InterQual Guidelines®, to assist us in administering health benefits. The InterQual Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. Other Policies and Coverage Determination Guidelines may also apply. UCare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary and to provide benefits otherwise excluded by medical policies when necessitated by operational considerations.”
POLICY DESCRIPTION:

This policy describes the use of autologous chondrocyte implantation (ACI), also called autologous chondrocyte transplantation (ACT), for the repair of defects in the articular cartilage of the knee. ACI may slow the progression of tissue damage, thus delaying partial or total joint replacement surgery. The goal of ACI is to provide pain relief, thereby allowing people suffering from articular cartilage damage to regain mobility and return to an active life.

COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:

Autologous chondrocyte implantation (ACI), also called autologous chondrocyte transplantation (ACT), is considered PROVEN and MEDICALLY NECESSARY for single, symptomatic, full-thickness articular cartilage defects when all the following are present:

- Patient is between ages of 18 to 55 years,
- Defect is greater than 2 squared cm,
- Defect is in the articular cartilage of the femoral condyle (medial, lateral, or trochlear),
- Has a body mass index (BMI) less than or equal to 35,
- Patient has had an inadequate response to prior arthroscopic or other surgical repair,
- Patient has failed to respond to conservative treatment, including but not limited to:
  - Physical therapy,
  - Braces,
  - Nonsteroidal anti-inflammatory drugs (NSAIDS),

Autologous chondrocyte implantation, also called autologous chondrocyte transplantation, is considered EXPERIMENTAL AND INVESTIGATIONAL and not medically necessary for indications other than those listed as proven and medically necessary due to insufficient published, scientific, peer-reviewed literature regarding safety and efficacy or improved patient outcomes. This includes, but is not limited to, the following indications:

- Cartilage defects in locations other than the femoral condyle of the knee,
- Children (growth plates have not closed),
- Partial-thickness defects,
- Multiple defects,
- Defects of the patella,
- Osteochondritis dissecans,
- Previous history of cancer in the bones, cartilage, fat or muscle of the treated limb,
- Treatment of cartilage damage associated with generalized osteoarthritis,
- Pre-existing conditions, including meniscus tears, joint instability, or malalignment, unless these conditions are assessed and treated prior to or concurrent with autologous chondrocyte implantation.
### Clinical Considerations:

ACI is approved as a second-line treatment in the United States (FDA 1997).

Carticel product is contraindicated in patients with a known history of hypersensitivity to gentamicin, other aminoglycosides, or materials of bovine origin (components of the chondrocyte culture medium). Carticel is not indicated for treatment of cartilage damage associated with generalized osteoarthritis or for patients with total meniscectomy, unless surgically reconstructed prior to or concurrent with Carticel implantation. It should not be used in patients who have had cancer in the bones, cartilage, fat, or muscle of the affected limb. The efficacy of ACI in young children and patients older than age 65 was not studied prior to Food and Drug Administration (FDA) approval; and the safety of ACI during pregnancy or breastfeeding has not been established (Genzyme Corp., 2013b).

Possible Complications: Graft failure rates range from 0% to 15% in recent studies. Graft failures have been attributed to poor compliance with the rehabilitation protocol or to events such as traumatic accidents. Arthroscopic evaluation of symptoms or surgery may be needed when symptoms occur. The risk of revision surgery may be increased for ACI with periosteal flap.

A decrease in the occurrence of adverse events over time and between iterations of ACI procedures has been observed, which may reflect better physician training and improved technology associated with surgical procedures (i.e., innovating from periosteal flaps to engineered membranes).

### BACKGROUND:

The knee joint includes 3 major articulations: between the femur and patella, between the lateral femoral and tibial condyles, and between the medial femoral and tibial condyles. The ends of these articulating bones are covered by hyaline cartilage, which is hard and smooth, is almost frictionless, can withstand heavy loads, and distributes mechanical shock to protect the underlying bone. Hyaline cartilage defects acquired through trauma or a degenerative process lead to pain in surrounding tissue, swelling, locking, and/or giving way of the knee. Hyaline cartilage appears to have little capacity for regeneration due to its avascular and relatively acellular composition. Articular surfaces that are damaged by trauma or degenerative processes fill in primarily or completely with fibrocartilage, but only when the subchondral plate is penetrated. Fibrocartilage does not have the biomechanical properties of hyaline cartilage, and degrades over time. Although natural repair with fibrocartilage can produce good short- and medium-term results, biological and epidemiological data suggest that it does not prevent long-term development of osteoarthritis.

Cartilage defects can be classified as chondral (cartilage loss) or osteochondral (OC) (cartilage plus bone loss) fractures. Chondral defects are categorized further into partial-thickness or full-thickness, the latter of which extends to the subchondral bone. Although partial-thickness defects do not always produce significant symptoms, over time they can become full-thickness defects and predispose an individual to osteoarthritis.

There is no standard approach to the treatment of hyaline cartilage defects in the knee. Nonoperative treatment, such as weight loss, physical therapy, nonsteroidal anti-inflammatory drugs, intra-articular injection of hyaluronic acid derivatives, etc. can be suboptimal or short-lasting. Cartilage defects may
progress to severe osteoarthritis making total knee replacement necessary.

Investigators have developed a number of techniques designed to replace or stimulate new cartilage. One strategy is to allow stem cells from the bone marrow to infiltrate the defect and differentiate into chondrocytes, which in turn produce new cartilage. However, the fibrocartilaginous tissue resulting from these methods cannot restore the biomechanical properties of normal articular tissue, and may eventually fail under repeated mechanical stress. Another approach involves various forms of allogenic or autologous grafting, which aim to fill defects with transplanted hyaline cartilage.

Autologous chondrocyte implantation (ACI), also known as autologous chondrocyte transplantation (ACT), aims to stimulate hyaline cartilage regeneration and fill defects with new hyaline tissue. The process involves removal, expansion (culture), and reimplantation of the patient’s own chondrocytes. The implant is covered with a periosteal flap (ACI-P) or collagen membrane (ACI-C). These procedures both require extensive suturing to create an effective seal, and cell leakage is a potential problem. Matrix-induced autologous chondrocyte implantation (MACI) attempts to bypass this problem by using a membrane on which chondrocytes are seeded and cultured for several days, before the membrane is applied to the defect. These reimplanted chondrocytes have the potential to generate new hyaline or hyaline-like tissue with the goal of improving the quality of cartilage repair.

Alternatives to ACI include osteochondral (OC) grafting, in which a plug of bone and healthy cartilage is harvested from one area and transplanted to the injury site, mosaicplasty grafting in which one or more cylindrical osteochondral autografts are transferred from a low weight-bearing area of the knee to the defective site and microfracture surgery in which small holes are made in the bone near the damaged cartilage in an attempt to release cells that build new cartilage.

REGULATORY STATUS:

1. **U.S. FOOD AND DRUG ADMINISTRATION (FDA):** On August 22, 1997, the FDA granted a Biologics License for Carticel (Genzyme Corp.), approving autologous chondrocytes for the repair of clinically significant, symptomatic cartilaginous defects of the femoral condyle caused by acute or repetitive trauma. This was the first FDA license granted for a somatic cellular therapy and approval was contingent upon several requirements which were subsequently fulfilled. The current FDA-approved indication for Carticel is for the repair of symptomatic, cartilaginous defects of the femoral condyle (medial, lateral, or trochlear), caused by acute or repetitive trauma, in patients who have had an inadequate response to prior arthroscopic or other surgical repair (FDA 1997). On June 21, 2007, the FDA notified Genzyme that postmarketing study requirements had been satisfied by the Study of the Treatment of Articular Repair (STAR) (Zaslav et al., 2009), a prospective, longitudinal, multicenter study involving 154 patients with inadequate response to previous non-Carticel surgical treatment of cartilage defects in the medial, lateral or trochlear condyles (FDA 2007).

2. **CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):** Medicare does not have a National Coverage Determination (NCD) for autologous chondrocyte implantation to the knee. Local Coverage Determinations (LCDs) do exist.
3. MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):
Minnesota DHS does not have a policy statement for autologous chondrocyte implantation to the knee in its Provider Manual or other specific provider references.

CLINICAL EVIDENCE:
The literature search yielded 17 publications derived from 12 studies for detailed review. In the 17 publications, ACI was compared with surgical procedures such as abrasion, autologous osteochondral (OC) grafting, debridement, microfracture, mosaicplasty, and OC autograft transfer, with microfracture as the most common comparator. This body of evidence and its conclusions apply most directly to first- and second-generation ACI procedures (with periosteal flap [ACI-P] or collagen membrane flap [ACI-C], respectively).

SUMMARY:
Twelve comparison trials of varying quality, using somewhat heterogeneous outcome measures, suggested that ACI provides short-term outcomes comparable to those provided by other surgical options, such as osteochondral grafting, mosaicplasty and microfracture surgery for second-line treatment of full-thickness defects in the articular cartilage of the knee. Some studies suggested that improvements in ACI groups were durable over time.

There was no evidence from either randomized trials or observational studies regarding the long-term effectiveness of ACI. This does not rule out the possibility of a long-term effect, since most of the studies were limited by follow-up intervals of < 5 years. Full participation in high-impact activities usually resumes after 2 years; the 10-year follow-ups will likely provide valuable information about durability and clinical improvement. The presumed advantage of hyaline cartilage regeneration for preventing premature osteoarthritis would not be realized for at least 20 years (the patients in the reviewed studies were typically still in their 30s). Very limited and nonsystematic biopsy data suggest that most first-time ACI procedures produce some new hyaline or hyaline-like cartilage. These data corroborate the rationale for ACI but do not prove that long-term outcomes are enhanced compared with other surgical options.

APPLICABLE CODES:
The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

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<th>HCPCS Codes</th>
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<tr>
<td>J7330</td>
<td>Autologous cultured chondrocytes, implant</td>
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<td>S2112</td>
<td>Arthroscopy, knee, surgical for harvesting of cartilage (chondrocyte cells)</td>
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<td>715.16</td>
<td>Osteoarthrosis, localized, primary, lower leg</td>
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<td>715.26</td>
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### ICD-10 Codes

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<td>M23</td>
<td>Internal derangement of knee</td>
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<td>M93.26</td>
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<td>M94.9</td>
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### CPT® Codes

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<td>27412</td>
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<td>29870</td>
<td>Arthroscopy, knee, diagnostic, with or without synovial biopsy (separate procedures)</td>
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### REFERENCES:


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<td>05-28-2015</td>
<td>Reviewed and approved by the Quality Improvement Advisory and Credentialing Council (QIACC).</td>
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<tr>
<td>07-1-2015</td>
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