AUTOLOGOUS CHONDROCYTE TRANSPLANTATION
IN THE KNEE

Policy Number: SURGERY 006.17 T2

INSTRUCTIONS FOR USE

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CONDITIONS OF COVERAGE

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<th>Applicable Lines of Business/ Products</th>
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¹Precertification with review by a Medical Director or their designee is required.
BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Essential Health Benefits for Individual and Small Group
For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Autologous chondrocyte transplantation (ACT) is proven and medically necessary for treating patients with a single symptomatic full-thickness articular cartilage defect when ALL of the following criteria are met:
- Adult younger than age 55,
- Defect is greater than 2 squared cm,
- Defect is caused by acute or repetitive trauma,
- Defect is in the articular cartilage of the femoral condyle (medial, lateral, or trochlea),
- Member has had an inadequate response to a prior arthroscopic or other surgical repair procedure (e.g., debridement, microfracture, drilling/abrasion arthroplasty, or osteochondral allograft/autograft), and
- Member has failed to respond to conservative treatment such as physical therapy, braces, and/or nonsteroidal anti-inflammatory drugs (NSAIDs).

Autologous Chondrocyte Transplantation is considered unproven and not medically necessary for treating patients with the following indications:
- Patients who have cartilage defects in locations other than the femoral condyle of the knee,
- Patients whose growth plates have not closed,
- Patients who have partial-thickness defects,
- Patients with history of multiple defects,
- Patients with history of defects of the patella,
- Patients who have osteochondritis dissecans,
- Patients who have had previous history of cancer in the bones, cartilage, fat or muscle of the treated limb,
- Osteoarthritis,
- Patients with unstable knee,
- Total meniscectomy,
- Inflammatory diseases of the joint

There is insufficient evidence to conclude that ACT is beneficial for health outcomes in patients with osteochondritis dissecans, osteoarthritis, or for cartilage defects.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

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Normal articular cartilage is a complex tissue composed of matrix, chondrocytes and water. The chondrocytes are responsible for synthesizing the matrix, which is composed primarily of collagen fibers, hyaluronate, and sulfated proteoglycans. Articular cartilage damaged through acute or chronic trauma or osteochondritis dessecans, has limited ability to regenerate, leading to the symptoms of pain, restricted mobility and locking. When a full-thickness cartilage injury occurs, the articular surface does not usually regenerate on its own. Surgical treatment options include autologous chondrocyte transplantation.

Autologous chondrocyte transplantation, also referred to as autologous chondrocyte implantation, is a form of tissue engineering that creates a graft from a patient's own cartilage cells to repair defects in the articular cartilage.

Most patients are referred for autologous chondrocyte implantation after already having had surgery for an articular cartilage problem. If the patient remains symptomatic, and the patient and the surgeon decide that autologous chondrocyte implant is the best option, then an arthroscopic biopsy is planned.

ACI is a two-step procedure. New cartilage cells are grown and then implanted in the cartilage defect. The process involves removal, expansion (culture), and reimplantation of the patient's own chondrocytes. The procedure involves the collection and culture of articular cartilage cells (i.e., chondrocytes). With the patient under general anesthesia, an arthrotomy is performed, the cultured cells are placed into the cartilage defect, and held in place with a periosteal patch. Repair of ligamentous or other soft tissue structures may be performed concurrently, as needed. The chondrocytes are then implanted into the defect with the goal of generating new hyaline or hyaline-like tissue which will repair the articular surface. After the initial non-weight-bearing period immediately following surgery, an intensive physical rehabilitation program is initiated, with a gradual increase in weight bearing, and return to full activities.

**CLINICAL EVIDENCE**

Oussedik et al (2015) performed a systematic review of the treatment of articular cartilage lesions of the knee by microfracture or ACI to determine the differences in patient outcomes after these procedures. These investigators searched PubMed/Medline, Embase, and The Cochrane Library databases in the period from January 10 through January 20, 2013, and included 34 articles in this qualitative analysis. All studies showed improvement in outcome scores in comparison with baseline values, regardless of the treatment modality. The authors concluded that microfracture appeared to be effective in smaller lesions and is usually associated with a greater proportion of fibrocartilage production, which may have an effect on durability and eventual failure. Autologous chondrocyte implantation is an effective treatment that may result in a greater proportion of hyaline-like tissue at the repair site.

Harris et al. (2010) conducted a systematic review to compare autologous chondrocyte implantation with other cartilage repair or restoration techniques. Thirteen studies (n =917) were included. Patients underwent autologous chondrocyte implantation (n = 604), microfracture (n = 271), or osteochondral autograft (n = 42). Three of 7 studies showed better clinical outcomes after autologous chondrocyte implantation in comparison with microfracture after 1 to 3 years of follow-up, whereas 1 study showed better outcomes 2 years after microfracture and 3 other studies showed no difference in these treatments after 1 to 5 years. Clinical outcomes after microfracture deteriorated after 18 to 24 months (in 3 of 7 studies). Autologous chondrocyte implantation and osteochondral autograft demonstrated equivalent short-term clinical outcomes, although there was more rapid improvement after osteochondral autograft (2 studies). A defect size of >4 cm (2) was the only factor predictive of better outcomes when autologous chondrocyte implantation was compared with a non-autologous chondrocyte implantation surgical technique. The authors concluded that all of the cartilage repair/restoration techniques provide short-term success.

A systematic review of 9 different trails (n=626) by Vasiliadis et al. (2010) found that ACI is an effective treatment for full thickness chondral defects of the knee, providing an improvement of clinical outcomes. The authors note, however, that there is insufficient data to say whether ACI is superior to other treatment strategies in full thickness articular cartilage defects of the knee. Additional studies are needed before specific clinical recommendations can be made.

Vavken and Samartzis (2010) conducted a systematic review of 9 studies (n=526) to compare ACI to other methods of cartilage repair or placebo. The authors found that there was no clear recommendation concerning the efficacy of ACI compared to other treatment options such as microfracture or osteochondral grafts. There is, however, some evidence for better clinical outcomes for ACI compared with osteochondral grafts and equivalent outcomes compared with microfracture. Additional studies are needed to further assess the benefits of ACI compared to other treatments.

A systematic review conducted by authors at Vanderbilt University attempted to define the comparative effectiveness of, and indications for, ACI and osteochondral autograft transfer system (OATS) to treat full-thickness (Outerbridge stage 3 or 4) defects (Magnussen et al., 2008). The review included four trials (Bentley et al., 2003; Horas et al., 2003; Knutsen et al., 2004; Visna et al., 2004), a comparison of ACI using collagen membrane cover (ACI-C) with
matrix-guided ACI (MACI), and a comparison of autologous osteochondral grafting with microfracture. The authors were not able to demonstrate a clear superiority of one procedure over the other.

A Cochrane Review by Wasiak et al. (2006) concluded that evidence was insufficient to determine whether ACI was superior to other treatment options for full-thickness cartilage lesions of the knee.

Another Cochrane Review by Vassiliadis and Wasiak (2010) concluded that there was insufficient evidence to draw conclusions on the use of ACI for treating full thickness articular cartilage defects in the knee.

Basad et al. (2010) compared the clinical outcomes of patients with symptomatic cartilage defects treated with matrix-induced autologous chondrocyte implantation (MACI) or microfracture (MF). The 60 patients included were 18 to 50 years of age with symptomatic, post-traumatic, single, isolated chondral defects (4-10 cm2) and were randomized to receive MACI (40) or MF (20). Patients were followed up 8-12, 22-26 and 50-54 weeks post-operatively for efficacy and safety evaluation. The difference between baseline and 24 months post-operatively for both treatment groups was significant for the Lysholm, Tegner, patient ICRS and surgeon ICRS scores. However, MACI was significantly more effective over time (24 months versus baseline) than MF according to the Lysholm, Tegner, ICRS patient and ICRS surgeon scores. According to the authors, MACI is superior to MF in the treatment of articular defects over 2 years.

Zeifang et al. (2010) evaluated whether matrix-associated autologous chondrocyte implantation or the original periosteal flap technique provides superior outcomes in terms of clinical efficacy and safety. Twenty-one adult patients (mean age, 29.3 ± 9.1 years) with symptomatic isolated full-thickness cartilage defects (mean 4.1 ± 09 cm2) at the femoral condyle were randomized to matrix-associated autologous chondrocyte implantation or the original periosteal flap technique. The primary outcome parameter showed improvement of patients 1 year after autologous chondrocyte implantation, but there was no difference between the periosteal flap technique and matrix-associated ACI; 2 years after ACI, a similar result was found. The authors concluded that there was no difference in the efficacy between the original and the advanced ACI technique 12 and 24 months after surgery regarding International Knee Documentation Committee, Tegner Activity Score, and Short Form-36; however, with respect to the Lysholm and Gillquist score, better efficacy was observed in the periosteal flap technique group.

Comparative results varied according to the comparison surgery. Fu et al. (2005) observed that at 3 years, Cincinnati Knee Rating System (CKRS) scores were 2 to 3 points higher (on 10-point scales) in the ACI group than in the debridement alone group, both for overall condition and for individual symptoms. The difference in overall scores was significant. However, this was a retrospective study and CKRS data were missing for 28% to 60% of debridement patients, depending on the individual measure. Furthermore, the study did not differentiate between first- and second-line use of ACI, and several other aspects of the study design introduced bias.

In the comparisons with narrow stimulation, improvements in pain and various functional measures were either comparable between the two types of procedures or slightly better following abrasion or microfracture than following ACI (Knutsen et al., 2004; Visna et al., 2004; Knutsen et al., 2007; Saris et al., 2008). This was true of both 5-year and more short-term outcomes. These studies represented moderately strong evidence, but baseline differences in the study by Saris and colleagues created a small bias in favor of microfracture.

Saris et al. (2009) evaluated clinical outcome at 36 months after characterized chondrocyte implantation (CCI) versus microfracture (MF). Based on the results of the trial, the authors concluded that characterized chondrocyte implantation for the treatment of articular cartilage defects of the femoral condyles of the knee results in significantly better clinical outcome at 36 months in a randomized trial compared with MF. Time to treatment and chondrocyte quality were shown to affect outcome.

Results were less consistent for comparisons with autologous osteochondral grafting. Differences between ACI procedures and a mix of single and multiple osteochondral grafting procedures slightly favored osteochondral grafting (Horas et al., 2003). This study also represented a mix of first-line and second-line applications; results were not reported separately. Mean defect size was 3.75 cm2. Bentley et al. (2003) reported results that favored ACI: 88% of ACI recipients and only 69% of mosaicplasty recipients had a good or excellent overall modified CKRS score at 19 months. However, mean defect size in this study was relatively large (4.66 cm2), and one critic suggested that some patients may not have been appropriate candidates for mosaicplasty (Kish and Hangody, 2004). In the study by Dozin et al. (2003), outcomes were considerably better in the mosaicplasty group: 68% patients had a Lysholm score of 90 or more, compared with 46% of ACI patients. Significance testing was not reported, follow-up was less than 1 year, and the study had several other significant weaknesses. This study differed from the other two osteochondral grafting comparisons in that it involved first-line rather than second-line application and mean lesion size was smaller. Mean defect size was approximately 2 cm2, consistent with guidelines for mosaicplasty reported in review articles (Clar et al., 2005; Vanlauwe et al., 2007).
A case series by Peterson et al. (2010) evaluated the clinical outcomes of autologous chondrocyte implantation in 224 patients 10 to 20 years after implantation (mean = 12.8 years). The authors found that autologous chondrocyte implantation is an effective and durable solution for the treatment of large full-thickness cartilage and osteochondral lesions of the knee joint and clinical and functional outcomes remain high even 10 to 20 years after the implantation.

**Best Candidates for ACI**

Scientific literature reflects the following consensus regarding the best selection criteria for ACI (Clar et al., 2005; Lewis et al., 2006; Vanlauwe et al., 2007; Brittberg, 2008):
- Adults younger than 55 years who will return to a relatively high activity level.
- Symptomatic lesion.
- Single, contained (healthy articular cartilage at lesion border), unipolar (no lesion on opposing surface), full thickness defect > 2 cm² (Some authors recommend ACI as an alternative to marrow stimulation if the lesion is uncontained.)
- No significant bone loss.
- Full range-of-motion, intact ligaments and physiologically correct lower limb axis (corrective procedures may be performed in combination with or prior to ACI).
- No osteoarthritis of the knee, autoimmune connective tissue disease, active rheumatoid arthritis, or malignancy.
- Patient motivated and willing to comply with rigorous rehabilitation program.

Bony defects greater than 8 mm should be corrected with bone grafts before chondrocyte implantation.

**Adverse Events and Complications**

Studies involving 75 or more autologous chondrocyte implantation (ACI) procedures (total n=540 patients) reported failure rates of 4% to 13%, depending on how failure is defined and depending on where procedures are performed (Peterson et al., 2000; Minas, 2001; Browne et al., 2005). Adverse events were generally reported in terms of the need for arthroscopic evaluation of symptoms or for subsequent surgery. Such a need occurred in 25% to 65% of patients (nonuniform follow-up intervals). Symptomatic complications related to the periosteal flap were by far the most common adverse effects, prompting arthroscopic investigation in 20% to 26% of study participants (Peterson et al., 2000; Minas, 2001) and accounting for 10% of subsequent surgeries among ACI successes (Browne et al., 2005) or 51% of all subsequent surgeries (Henderson et al., 2006). Flap-related complications included both periosteal hypertrophy and implant extrusion.

Another review by Wood et al. (2006) found that the most common adverse events following Carticel implantation included graft failure, delamination, and tissue hypertrophy. Graft failures have been attributed to poor compliance with the rehabilitation protocol or to events such as traumatic accidents.

**ACI in Adolescents**

Some experts believe the use of ACI in children is not reasonable, since regenerative capacities are so much greater than in adults and due to potential interference epiphysis closure (Vanlauwe et al., 2007). However, other authors have seen the potential for faster healing to be a good reason to try ACI in athletes. A review of 37 adolescent (age 11-17) ACI procedures listed in the Cartilage Repair Registry showed an 88% rate of good/excellent outcomes (Micheli et al., 2006).

DiBartola et al., 2016 performed a systematic review of the use of autologous chondrocyte implantation in the adolescent knee. PubMed, MEDLINE, SCOPUS, CINAHL, and Cochrane Collaboration Library databases were searched systematically. Outcome scores recorded included the International Knee Documentation Committee score, the International Cartilage Repair Society score, the Knee Injury and Osteoarthritis Outcome Score, the visual analog scale, the Bentley Functional Rating Score, the Modified Cincinnati Rating System, Tegner activity Lysholm scores, and return athletics. Outcome scores were compared among studies based on proportion of adolescents achieving specific outcome quartiles at a minimum 1-year follow-up. The authors concluded that cartilage repair in adolescent knees using ACI provides success across different clinical outcomes measures. The only patient- or lesion-specific factor that influenced clinical outcome was the shorter duration of preoperative symptoms.

**ACI for Trochlear and Patellar Defects**

Published trials comparing ACI with other surgical repair procedures for defects in the knee included relatively few patients with trochlear or patellar defects. A review of 40 Cartilage Repair Registry patients who underwent ACI for trochlear cartilage defects reported positive outcomes (Mandelbaum et al., 2007). In most cases, ACI followed previous attempts at surgical repair, often marrow stimulation. Defects were generally large (mean 4.5 cm²). A longitudinal study separately analyzed results for 45 patients who underwent ACI for defects on the patella, trochlea, patella plus trochlea, weight bearing condyle plus patella, weight bearing condyle plus trochlea, or weight bearing condyle plus patella plus trochlea (Minas and Bryant, 2005). Affected patellar surface averaged 4.86 cm², and affected trochlear surface averaged 5.22 cm². Most (71%) patients reported a good or excellent overall outcome. However, the rate of graft failure was rather high (18%).
In the only study that provided results according to defect type (Bentley et al., 2003), between-group differences for defects on the patella and trochlea were similar to those for femoral defects. The number of patients in those categories was very small. No results specific to osteochondritis dissecans (OCD) were presented by any study.

**Additional Applications**

A review on “Surgical therapy of osteoarthritis” (Kalunian, 2014) states that “Replacing localized regions of degenerated cartilage with autologous chondrocyte grafts has not been studied in large groups of patients. It is unlikely that this technique will be helpful in patients with advanced joint degeneration because of the large surface area that needs grafting in this setting. Replacing localized regions of degenerated cartilage with autologous chondrocyte grafts may be beneficial for selected patients with less severe, localized articular cartilage defects, but it requires further study”. Additional research is needed to expand the knowledge of and develop guidelines for management of chondral injuries of the hip.

Current evidence regarding ACI largely examines cartilage restoration of the knee joint. However, two small studies and one case report were identified in the literature that evaluated the use of ACT in other joints. Investigators assessed the use of autologous chondrocytes in osteochondral lesions of the ankle joint and osteochondrosis dissecans of the ankle joint (n=8; n=8). In the first study, at 2 years of follow-up, both subjective and objective clinical improvement was observed in all patients. (Giannini, 2001) Arthroscopy and histological analysis revealed cartilaginous tissue covering the lesion area, although cell numbers were increased compared with normal cartilage. Koulalis et al. (2002) reported good to excellent results in the postoperative evaluation scores, with no complications. Arthroscopic examinations in 3 patients revealed the existence of cartilage-like tissue with complete coverage of the chondral effect. Romeo et al. (2002) reported on the use of ACT in the repair of an articular defect in the humeral head of a young patient. After 12 weeks, the patient demonstrated full range of painless motion with no complaints of rest pain or weather-related pain. Despite these early clinical results, the available scientific evidence does not allow definitive conclusions regarding the safety and efficacy of ACT in treating focal defects of joints other than the knee, such as ankle, hip, wrist, or shoulder.

Jordan et al (2012) performed a systematic review of clinical outcomes following various treatments for chondral lesions of the hip and defined the techniques for the treatment of these cartilage defects. The full manuscripts of 15 studies were reviewed for this systematic review including case studies, case series, and clinical studies. A variety of techniques have been reported for the treatment of symptomatic chondral lesions in the hip. Although good results have been reported, most studies lacked both a control group and a large number of patients. The authors concluded that the findings in this article do provide a good foundation for treatments and stimulant for further study in an inherently difficult to treat young patient population with articular cartilage defects in the hip.

According to Hayes, there is insufficient evidence to evaluate the clinical effectiveness of autologous chondrocyte implantation compared with nonsurgical treatment. However, seven comparison trials of varying quality suggested that ACI provides short-term outcomes comparable to those provided by other surgical options for second-line treatment of full-thickness defects in the articular cartilage of the knee. Four moderately large non comparison studies suggested that autologous chondrocyte implantation poses no serious safety issues. However, in its original form, autologous chondrocyte implantation often requires follow-up arthroscopic correction of hypertrophy and even high-volume centers have reported that implants can fail completely. There was no evidence from either randomized trials or observational studies regarding the long-term effectiveness of autologous chondrocyte implantation. This does not rule out the possibility of a long-term effect since most of the studies were limited by follow-up intervals of less than 2 years. Very limited and nonsystematic biopsy data suggest that most first-time autologous chondrocyte implantation procedures produce some new hyaline or hyaline-like cartilage. These data corroborate the rationale for autologous chondrocyte implantation but do not prove that long-term outcomes are enhanced compared with other surgical options. Given the typical characteristics of lesions included in the studies, the evidence more strongly supports use of ACI for lesions of the femoral condyle than for lesions in other locations. Although the FDA-approved indication for ACI is restricted to traumatic lesions, not all studies observed this restriction and results were not reported separately by etiology. Only studies with long-term follow-up, in the range of 20 years or more, will provide final answers to questions about the presumed superior ability of ACI to produce hyaline or hyaline-like cartilage and to prevent premature osteoarthritis. Such data can then also be used to clarify which patients and what types of lesions are most likely to benefit from ACI as opposed to another surgical technique. (Hayes, 2013)

In a prospective cohort study, Kon et al. (2009) compared the clinical outcome of patients treated with second-generation Hyalograft C autologous chondrocyte implantation implants (n=40) with those treated with the microfracture repair (n=40). All patients had grade III to IV cartilage lesions of the femoral condyles or trochlea. Both groups demonstrated statistically significant improvement of all clinical scores from preoperative interval to 5-year follow-up. When comparing the groups, better improvement of the International Knee Documentation Committee objective (P < .001) and subjective (P = .003) scores was observed in the Hyalograft C group at 5-year follow-up. The return to sports at 2 years was similar in both groups and remained stable after 5 years in the Hyalograft C group; it...
worsened in the microfracture group. The investigators concluded that better clinical results and sport activity resumption were demonstrated in the group treated with second-generation autologous chondrocyte transplantation.

Zaslav et al. (2009) assessed the effectiveness of autologous chondrocyte implantation in a prospective clinical study of patients who failed prior treatments for articular cartilage defects of the knee. Follow-up was 48 months. One hundred twenty-six patients (82%) completed the study protocol. Seventy-six percent of patients were treatment successes at the end of the study and 24% were identified as treatment failures. Mean improvements were observed from baseline to all time points (P < .001) for all outcome measures. Preoperative to 48-month values, respectively, were as follows: On the Knee injury and Osteoarthritis Outcome Score subscales of pain: 48.7 to 72.2; other symptoms: 51.8 to 70.8; sports/recreation: 25.8 to 55.8; knee quality of life: 20.9 to 52.2; and activities of daily living: 58.6 to 81.0; on the Modified Cincinnati Overall Knee score: 3.3 to 6.3; on the visual analog scale: 28.8 to 69.9; and on the SF-36 Overall Physical Health: 33.0 to 44.4. Results did not differ between patients whose primary surgery had been a marrow-stimulating procedure and those whose primary procedure had been a debridement alone. The median difference in duration of benefit between autologous chondrocyte implantation and the failed non-autologous chondrocyte implantation prior procedure was at least 31 months (P < .001). Seventy-six patients (49%) had subsequent surgical procedure(s), predominantly arthroscopic. The investigators concluded that patients with moderate to large chondral lesions with failed prior cartilage treatments can expect sustained and clinically meaningful improvement in pain and function after autologous chondrocyte implantation. The subsequent surgical procedure rate observed in this study (49% overall; 40% related to autologous chondrocyte implantation) appears higher than generally reported after autologous chondrocyte implantation.

Niemeyer et al. (2008) reported the clinical results obtained in 70 patients treated with ACI for full-thickness defects of the patella. At a mean follow-up of 38.4 months, patients' subjective functional knee scores (IKDC, Lysholm) were analyzed, as were the results of objective examination (according to International Cartilage Research Society [ICRS]). The mean Lysholm score at the time of follow-up was 73.0 (+/-22.4) and the subjective IKDC score was 61.6 (+/-21.5); normal and nearly normal clinical results according to ICRS were achieved in 67.1% of the patients, while abnormal results were achieved in 20.0% of the patients and severely abnormal results, in 12.9% of the patients.

### Professional Societies/Organizations

**American Academy of Orthopaedic Surgeons (AAOS)**

In a 2010 clinical practice guideline on the diagnosis and treatment of osteochondritis dissecans (OCD), the American Academy of Orthopaedic Surgeons (AAOS) was unable to recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable osteochondritis dissecans lesion.

**National Institute for Health and Clinical Excellence (NICE)**

Current NICE Guidance recommends 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 outcome data, including the measurement of health-related quality of life and long-term follow-up. (NICE, 2008)

### U.S. FOOD AND DRUG ADMINISTRATION (FDA)

**Carticel**: The culturing of chondrocytes is considered by the FDA to fall into the category of manipulated autologous structural cells (MAS), which are subject to a biologic licensing requirement. At the present time, only Carticel™ (Genzyme) has received FDA approval for the culturing of chondrocytes through a biologics license.

On August 22, 1997, the FDA granted a Biologics License for Carticel®, approving it for provision of autologous chondrocytes for the repair of clinically significant, symptomatic cartilaginous defects of the femoral condyle caused by acute or repetitive trauma. The FDA granted a supplement to the Biologics License for Carticel on March 2, 2000. In response to a request made by Genzyme, the FDA narrowed the indication for use of autologous cultured chondrocytes to second-line therapy for patients who have failed other therapies.

The current FDA-approved indications for Carticel state that Carticel is indicated for the repair of symptomatic cartilage defects of the femoral condyle (medial, lateral or trochlea), caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure (e.g., debridement, microfracture, drilling/abrasion arthroplasty, or osteochondral allograft/autograft).

Carticel should only be used in conjunction with debridement, placement of a periosteal flap and rehabilitation.

Carticel is not indicated for:
- Treatment of cartilage damage associated with generalized osteoarthritis
- Patients with total meniscectomy unless surgically reconstructed prior to or concurrent with Carticel implantation
Prescribing information for Carticel specifies administration only by physicians who have completed Genzyme Biosurgery's Surgeon Training Program.

Pre-existing conditions, including meniscal tears, joint instability, or malalignment should be assessed and treated prior to or concurrent with Carticel implantation. Carticel should not be used in patients who have previously had cancer in the bones, cartilage, fat or muscle of the treated 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.


**REFERENCES**

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2016T0030N]


Kalunina KC. Surgical therapy of osteoarthritis. Last reviewed December 2014. UpToDate Inc., Waltham, MA.


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<td>• Updated benefit considerations; added instruction to check the member specific benefit plan document and any federal or state mandates, if applicable, before using this policy</td>
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<td>• Updated coverage rationale:</td>
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<td>o Replaced language indicating “autologous chondrocyte transplantation (ACT) is proven and medically necessary in members with a single symptomatic full-thickness articular cartilage defect when all of the [listed criteria] are present” with “autologous chondrocyte transplantation (ACT) is proven and medically necessary for treating patients with a single symptomatic full-thickness articular cartilage defect when all of the [listed] criteria are met”</td>
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<td>o Added language to indicate autologous chondrocyte transplantation is considered unproven and not medically necessary for treating patients with the [listed] indications</td>
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<td>• Updated supporting information to reflect the most current description of services, clinical evidence, FDA information, and references</td>
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