Autologous Chondrocyte Transplantation or Implantation
Corporate Medical Policy

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Description/Summary

Autologous chondrocyte implantation (ACI) is a method of resurfacing articular cartilage defects. The procedure involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral defect.

Policy

Coding Information
Click the links below for attachments, coding tables & instructions.
Attachment I- CPT Code Table & Instructions
Attachment II- ICD-10 Diagnosis code table

When service or procedure is medically necessary

Autologous chondrocyte implantation may be considered medically necessary for the treatment of disabling full-thickness articular cartilage defects of the knee (grade III or IV) of the weight bearing surface of the knee (medial or lateral femoral condyles or trochlear region) caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior surgical procedure, when all of the following criteria are met:

- 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);
- Focal, full-thickness (grade III or IV) unipolar lesions on 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;
When service or procedure is considered investigational

Autologous chondrocyte implantation for all other joints, including talar, and any indications other than those listed above is considered investigational.
Matrix-induced autologous chondrocyte implantation is considered investigational.

Policy Guidelines

For smaller lesions (e.g., < 4 cm²), if debridement is the only prior surgical treatment, consideration should be given to marrow-stimulating techniques before autologous chondrocyte implantation 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, e.g., body mass index (BMI) greater than 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. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

The entire autologous chondrocyte implantation (ACI) procedure consists of four steps: 1) the initial arthroscopy and biopsy of normal cartilage, 2) culturing of chondrocytes, 3) a separate arthrotomy to create a periosteal flap and implant the chondrocytes, and 4) post-surgical 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 (i.e. arthrotomy) is scheduled. There is a specific CPT category I code for ACI of the knee: 27412: Autologous chondrocyte implantation, knee.

Arthroscopic harvesting of chondrocytes from the knee is reported using CPT code 29870. There is a HCPCS code for the autologous cultured chondrocyte implant - J7330.

Information required

The request must be accompanied by supporting documentation of medical necessity, which includes; member’s name and age, symptoms and duration, previous conservative treatments and outcomes, results of prior arthroscopic or surgical repairs including photographs of the defect (may be obtained at time of chondrocyte harvesting), grade level of the defect, size of the cartilage defect, patient’s ability to comply with post-surgical rehabilitation.

Background

Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral
defect under a periosteal or fibrin patch. Second- and third-generation techniques include combinations of autologous chondrocytes, scaffolds, and growth factors.

The evidence for ACI for individuals who have focal articular cartilage lesions of the knee includes randomized controlled trials (RCTs) and prospective observational studies. Relevant outcomes are symptoms, functional outcomes, implant survival, quality of life, and resource utilization. Although evidence from long-term studies is still accumulating, current evidence indicates that Food and Drug Administration–approved ACI products can improve symptoms in some patients with lesions of the articular cartilage of the knee. These patients, who are too young for total knee replacement, have limited options. Therefore, ACI may be considered an option for large disabling full-thickness chondral lesions of the knee caused by acute or repetitive trauma. Evidence indicates that a prior surgical procedure may negatively impact the success of ACI, but ACI combined with meniscal allograft results in outcomes similar to either procedure performed alone. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence on ACI for individual who have focal articular cartilage lesions in joints other than the knee is limited. Relevant outcomes are symptoms, functional outcomes, implant survival, quality of life, and resource utilization. The greatest amount of literature is for ACI of the talus. A systematic review found that outcomes following treatment with ACI were inferior to microfracture. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input was requested on multiple occasions, most recently in 2015 for the use of ACI in the patella. Prior clinical input supported use for localized chondral defects when other treatments have not been successful. The most recent clinical input was generally supportive of the use of ACI for large patellar lesions, although there was a range in the degree of support. Reviewers indicated that outcomes were improved when realignment procedures were performed concurrently with ACI of the patella, and that success rates were lower when using ACI after a prior microfracture. A majority of reviewers recommended that a prior surgical procedure not be required for lesions greater than 4 cm2.

**Regulatory Status**

The culturing of chondrocytes is considered by the U.S. Food and Drug Administration (FDA) to fall into the category of manipulated autologous structural (MAS) cells, which are subject to a biologic licensing requirement. At the present time, only Carticel™ (Aastrom Biosciences) has received FDA approval for the culturing of chondrocytes through a biologics license. In 1997, Carticel 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....” The labeled indication was revised in October 1999 to read as follows:

“Carticel is indicated 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 a prior arthroscopic or other
surgical repair procedure.”

Thus, the revised labeling suggests a more restricted use of autologous chondrocytes (ie, as a second-line therapy after failure of initial arthroscopic or surgical repair). “Carticel is not indicated for the treatment of cartilage damage associated with osteoarthritis. Carticel should only be used in conjunction with débridement, placement of a periosteal flap and rehabilitation. The independent contributions of the autologous cultured chondrocytes and other components of the therapy to outcome are unknown. Data regarding functional outcomes beyond 3 years of autologous cultured chondrocyte treatment are limited.”

A number of second-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development/testing or are available only outside of the United States. They include Atelocollagen (collagen gel; Koken), Bioseed® C (polymer scaffold; BioTissue Technologies) CaReS (collagen gel; Ars Arthro), Cartilix (polymer hydrogel; Biomet), Chondron (fibrin gel; Sewon Cellontech), Hyalograd C (hyaluronic acid-based scaffold; Fidia Advanced Polymers), MACI® (matrix-induced autologous chondrocyte implantation [ACI]; Aastrom Biosciences, available outside of the United States), NeoCart (ACI with a 3-dimensional chondromatrix; Histogenics, phase 3 trial), and Novocart®3D (collagen-chondroitin sulfate scaffold; Aesculap Biologics, phase 3 trial). ChondroCelect® (characterized chondrocyte implantation; TiGenix; phase 3 trial completed) 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 cartilage formation. Although clinical use of these second-generation ACI products has been reported in Europe and Asia, none is approved for use in the United States at this time.

Rationale/Scientific Background

This evidence review was based on a 2003 TEC Assessment of autologous chondrocyte implantation (ACI), which updates earlier 1996, 1997, and 2000 TEC Assessments on the same subject. The 2003 TEC Assessment separately evaluated the data regarding ACI when performed as either a first-line or second-line therapy in various subgroups of patients. At the time of this TEC Assessment, only 1 ACI product (Carticel™) had been evaluated in the published literature.

Updated literature searches, conducted periodically between 2003 and May 12, 2015, identified the following published studies. Some of these studies used Carticel™, while others evaluated newer, second-generation ACI products. The evidence for the second-generation products is discussed separately from the evidence on Carticel™. The long-term efficacy of marrow stimulation techniques is also reviewed.

Marrow Stimulation Procedures
Montgomery et al reported a study of articular cartilage procedures of the knee from a national database of insurance billing records. There were 216 million orthopedic procedures identified over a 6-year period. For the 163,448 articular cartilage procedure codes reported over this period, 98% were microfracture (n=36,095) or chondroplasty (n=125,245). Efficacy of the microfracture technique was examined in a 2009 systematic review. Twenty-eight studies
First-Generation ACI (Carticel™) for Treatment of the Knee

Systematic Reviews
In 2015, Mundi et al reported a systematic review of level 1 studies of cartilage restoration of the knee. Included were 12 randomized trials with a total of 765 patients and a mean lesion size of 3.9 cm². Five trials compared ACI with marrow stimulation (3 were second-generation ACI), 3 compared ACI with osteoarthritis (OA), 1 trial compared OA with microfracture, and 3 trials compared different generations of ACI. Eleven of the 12 trials were conducted in Europe. Four trials reported significant differences in function with ACI versus marrow stimulation, however, meta-analysis showed no significant differences in pain or function between the 2 treatments at 24-month follow-up. The quality of the evidence was rated as poor to moderate, and only 4 trials reported a sample size calculation. Although meta-analysis could not be performed on the other comparisons, 5 of 6 trials found no significant difference in outcomes between ACI and OA or different generations of ACI. The percentage of grafts that failed and the relation between lesion size and success rate were not assessed in this review.

A 2011 systematic review by Harris et al included 13 RCTs and nonrandomized trials of 917 subjects who underwent ACI (n=604), microfracture (n=271), or osteochondral autograft (OA) (n=42). The mean study quality was rated as 54 of 100, with no studies considered of good or excellent quality, 7 considered fair, and 6 considered poor. Four studies compared different generations of ACI, finding no difference in outcomes but higher complication rates with open, periosteal cover, first-generation ACI. At 1- to 5-year follow-up, 3 of 7 studies showed better clinical outcomes after ACI in comparison with microfracture, 1 study showed better outcomes after microfracture, and 3 studies showed no difference in these treatments. Clinical outcomes after microfracture deteriorated after 18 to 24 months in 3 of 7 studies. Studies comparing ACI and OA showed similar short-term clinical outcomes, with more rapid improvement but an increase in arthrofibrosis and donor site morbidity following OA. Younger patients with a shorter preoperative duration of symptoms and fewer prior surgical procedures had the best outcomes after surgical intervention. A defect size greater than 4 cm² was the only factor predictive of better outcomes when ACI was compared with other surgical techniques.

Another publication by Harris et al in 2010 was a systematic review of combined meniscal allograft transplantation and cartilage repair/restoration. Six level IV studies (case series) with a total of 110 patients were included in the review. Patients underwent meniscal allograft transplantation with either ACI (n=73), osteochondral allograft (n=20), OA (n=17), or microfracture (n=3). All studies showed improvement in clinical outcomes at final follow-up compared with the preoperative condition. Outcomes were also compared with historical outcomes of each individual procedure performed in isolation. Four of the 6 studies found outcomes equivalent to procedures performed in isolation, while 2 studies found that outcomes with combined surgery were not as good as the historical controls. Across the 6 studies, 13 failures (12%) were reported; these included 11 isolated meniscal allograft
transplantation failures, 1 combined meniscal allograft and ACI failure, and 1 isolated ACI failure. Three knees with failed meniscal allograft transplantation were converted to total knee arthroplasty. Nearly 50% of the patients underwent 1 or more subsequent surgeries after combined meniscal allograft transplantation and cartilage repair/restoration procedures.

**Comparative Studies: ACI (Carticel™) Versus Marrow-Stimulating Techniques**

In an RCT of 80 patients randomized to ACI or microfracture of the knee (an arthroscopic marrow-stimulation procedure), Knutsen et al reported no significant differences in treatment groups at 2-year follow-up in macroscopic and histologic findings. The Lysholm Knee Scoring Scale (LKSS) and pain scores did also not significantly differ at 1 and 2 years. The Physical Component Summary score of the 36-Item Short-Form Health Survey (SF-36) was worse in the ACI group, which the authors suggested may have been related to the greater surgical involvement. Five-year follow-up on all 80 patients revealed 9 failures (23%) for both groups. There was a trend (p=0.10) for earlier failure in the ACI group (26 months vs 38 months, respectively) with no difference in subjective measures of pain or function between the ACI and microfracture groups. Thus, the more invasive ACI open surgical procedure was not associated with added clinical benefit.

In Visna et al, 50 patients with full-thickness, moderate-to-large chondral defects of 2.0 to 10.0 cm² of the femoral condyle, trochlea, or patella (43 cases due to injury) were randomized to Johnson abrasion techniques or ACI of the knee using a preparation of autologus chondrocytes with a fibrin tissue glue rather than a periosteal patch to seal the implanted chondrocytes. The study reported improvements after 12 months in the LKSS, International Knee Documentation Committee (IKDC), and Tegner activity scores, which were significantly better among the 25 ACI patients than the 25 patients in the abrasion group. Additional procedures (28 in the ACI group, 20 in the abrasion group) included anterior cruciate ligament (ACL) replacement, meniscectomy, and lateral release.

**Comparative Studies: ACI (Carticel™) Versus Osteochondral Autografts**

Horas et al reported 2-year follow-up on a study of 40 patients (18-42 years old) with an articular lesion of the femoral condyle (range, 3.2-5.6 cm²) who were randomly assigned to undergo either autologous chondrocyte transplant or osteochondral autografting. Eleven (28%) had prior surgical treatment. The authors reported that both treatments improved symptoms (85% of each group), although those in the OA group responded quicker. Histomorphologic evaluation of 5 biopsy specimens at 2 years or less after transplantation indicated that the osteochondral cylinders had retained their hyaline character, although the investigators noted a persistent interface between the transplant and the surrounding original cartilage. Evaluation of ACIs indicated a rigid, elastic tissue, with partial roughening and the presence of fibrocartilage.

Bentley et al randomized 100 consecutive patients with symptomatic lesions of the knee (average, 4.7 cm²; range, 1-12 cm²) to ACI or mosaicplasty. Seventy-four percent of lesions were on the femoral condyle, and 25% of lesions were on the patella. Ninety-four patients had undergone previous surgical interventions, and the average duration of symptoms before surgery was 7 years. Clinical assessment at 1 year showed excellent or good results in 98% of the ACI patients and in 69% of the mosaicplasty patients. The mosaicplasty plugs showed incomplete healing of the spaces between the grafts, fibrillation of the repair tissue, and disintegration of the grafts in some patients. This finding may be related to the unusual prominent placement of the plugs in this study,
which was intended to allow contact with the opposite articular surface. Arthroscopy at 1 year showed filling of the defects following ACI, but soft tissue was observed in 50% of patients. Biopsy specimens from 19 ACI patients revealed a mixture of hyaline and fibrocartilage. With 6 patients lost to follow-up at a minimum 10 years after the index surgery, repair was found to have failed in 17% of patients treated with ACI and 55% of patients treated with mosaicplasty.

Dozin et al reported results from a multicenter RCT in which ACI was compared with OA. Forty-four subjects (61% male, 39% female) ages 16 to 40 years (mean, 28.7±7.8 years), who had a focal, symptomatic chondral injury of Outerbridge grade III or IV with no previous surgical treatment, were randomly assigned to ACI or mosaicplasty 6 months after undergoing arthroscopic débridement. The average lesion size was 1.9 cm. Only 12 of 22 (54%) in the ACI group and 11 of 22 (50%) of the mosaicplasty group actually underwent the assigned procedure. Dropouts comprised 14 patients (32%) who reported spontaneous improvement following arthroscopy and did not undergo subsequent surgery, 5 who did not show up at the presurgery examination and could not be further traced, and 2 who refused surgery for personal reasons. Because of the substantial dropout rate, the original primary outcome measure, the mean LKSS score assessed 12 months postsurgery was converted into a scale in which improvement was categorized by proportions of responders (LKSS <60, LKSS 60-90, LKSS 90-100). With this scale, and including 10 patients who were cured by débridement (intention-to-treat analysis), the percentages of patients who achieved complete success were 89% (16/18 evaluable cases) in the mosaicplasty arm versus 68% (13/19 evaluable cases) in the ACI arm (test for trend, p=0.093). The high rate of spontaneous improvement after simple débridement raises questions about the appropriateness of additional surgical intervention in patients similar to those included in this trial. These results are not sufficient to permit conclusions regarding the effect of ACI on health outcomes compared with mosaicplasty or to demonstrate an independent effect of the use of ACI versus débridement and exercise rehabilitation.

Other Controlled Trials
Results from the Study of the Treatment of Articular Repair (STAR) trial have been published; they were previously available in the Carticel package insert and from a meeting presentation in July 2007.

STAR was a prospective, open-label, 4-year study in 154 patients (mean age, 35 years; 69% male) from 29 clinical centers. Each patient served as his or her own control, undergoing ACI after having failed or experienced an inadequate response to a prior cartilage repair procedure (eg, 78% underwent débridement, 29% microfracture, 12% subchondral drilling) on a distal femur index lesion (109 medial femoral condyle, 32 lateral femoral condyle, 46 trochlea). The median lesion size was 4.6 cm2 (range, 1-30 cm2), with 26% involving osteochondritis dissecans. Fifty patients (32%) had multiple lesions in the reference knee, and 29 (19%) received multiple cellular implants. Prior treatment inadequacy was defined as both patient and surgeon agreement that the patient’s symptoms or function required surgical retreatment of the defect and a patient’s rating of overall condition of the knee was a score of 5 or less, using the Modified Cincinnati Knee Rating System (MCKRS). In this group, the median time to meet the failure criteria was 3.4 months for the prior index procedure, with more than 90% of patients having failed within 10.3 months. Patients who met these criteria were treated with ACI and assessed every 6 months for up to 4 years.

The primary outcome, treatment failure for ACI, was defined as any of the following: (1)
patient underwent surgical retreatment that violated the subchondral bone or repeated ACI for the same index defect; (2) complete delamination or removal of the graft; or (3) a patient’s rating of the overall condition of the knee using the MCKRS knee score did not improve from the baseline over 3 consecutive 6-month time intervals. Withdrawals from the study were considered as failures at the last follow-up. The mean overall MCKRS score for the entire patient population at baseline was 3.3 (n=154), and 126 (82%) completed 4-year follow-up. Thirty-seven patients (24%) were considered failures; 11 failed based on the surgical failure criterion, and 26 failed based on the MCKRS criterion. Most of the 37 failures (92%) occurred within 30 months. At 48 months, three-fourths of all patients in the study (76%) showed good-to-excellent results, with a mean MCKRS score of 6.3 (n=115). Secondary outcome measures also showed improvement, including pain, symptoms, sports and recreation, knee-related quality of life, and activities of daily living. There was no relation between the size of the lesion at baseline and treatment outcomes with ACI.

Over half of the population (54%) experienced at least 1 serious adverse event secondary to ACI, and 40% of patients underwent subsequent surgical procedures on the index knee related to ACI. Adverse events included arthrofibrosis (16%), graft overgrowth (15%), chondromalacia or chondrosis (12%), graft complications (ie, fraying or fibrillation, 10%), graft delamination (6%), and joint adhesion (5%). Subsequent surgical procedures (regardless of relationship to ACI) included débridement of cartilage lesion (31%), lysis of adhesions (14%), other débridement (10%), meniscectomy (6%), loose body removal (5%), microfracture of the index lesion (5%), and scar tissue removal (5%). The most common cause for a subsequent surgical procedure was periosteal patch hypertrophy. Most (61%) patients who had a subsequent surgical procedure went on to have successful results, while 39% were eventually considered treatment failures. The results of the STAR trial suggest that ACI may improve knee symptoms and function in some patients with severe, debilitating, previously treated cartilage lesions of the distal femur for at least 4 years after the procedure. Additional surgical procedures may be expected.

Gooding et al randomized 68 patients with osteochondral defects (mean, 4.5 cm2; range, 1-12 cm2) of the femoral condyle (54%), trochlea (6%), or patella (40%) to ACI with either a periosteal or a collagen cover. At 2 years, 74% of the patients with the collagen cover had good-to-excellent results compared with 67% of the patients with the periosteal cover. Hypertrophy required shaving in 36% of patients treated with the periosteal cover. None of the collagen covers required shaving.

In 2012, Pestka et al reported a matched-pair comparison of ACI after failed microfracture versus ACI as a first-line treatment. A total of 56 patients were retrospectively matched for sex, age, defect size, and defect location. The average defect size was 4.65 cm2. Follow-up was conducted by mail, with a mean follow-up time of 48.0 months for ACI as a second-line treatment and 41.4 months for ACI as a first-line treatment. The failure rate was significantly greater when ACI was used as a second-line treatment (25% vs 3.6%), and there was a trend (p=0.058) for lower IKDC scores (58.4 vs 69.0). Two Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales (Pain and Activities of Daily Living) were significantly lower for second-line treatment; there was a trend for lower scores in the remaining subscales. The study had several limitations; one was a potential for selection bias if patients who responded poorly to microfracture also responded poorly to ACI. Time since symptom onset might also have been a factor. However, the results added to a growing body of literature suggesting inferior outcomes when ACI is performed following a failed microfracture.
Observational Studies
A variety of issues have been addressed with observational studies, including durability of the procedure, influence of age, comparison of femoral versus patellar defects, combination treatment with meniscal allograft, influence of prior marrow stimulation, and treatment of early OA. They are discussed next.

Browne et al published 5-year outcomes from 87 of the first 100 patients (40 centers, 87% follow-up) treated with ACI for lesions on the distal femur from the FDA-regulated Carticel safety registry maintained by Genzyme Biosurgery. The registry is a multicenter program initiated in 1995 and designed to longitudinally track changes in function and symptoms in patients treated with ACI or other cartilage repair procedures. Patients were an average of 37 years old, with a mean lesion size of 4.9 cm2 (range, 0.8-23.5 cm2). Seventy percent of the patients had failed at least 1 previous cartilage procedure. At 5 years following the index procedure, the average self-rated overall condition had improved from 3.2 (poor to fair) to 5.8 (fair to good), a 2.6-point improvement on the 10-point scale. Sixty-two patients (71%) reported improvement; 25 (29%) reported no change or worsening. Thirty-seven patients (42%) had 51 surgeries after ACI. The most common findings were adhesions (n=6), hypertrophic changes of the graft (n=5), loose bodies (n=4), loose or delaminated perioseal patch (n=4), and meniscal tears (n=4). In 2010, this group of investigators published 6- to 10-year follow-up (mean, 9.2 years) on 72 patients in the cartilage repair registry. Fifty-four patients (75%) met the eligibility criteria of the study, which included ACI treatment of lesions on the distal femur and improvement at the 1- to 5-year follow-up period. Of these 54 patients, 47 (87%) sustained a mean improvement of 3.8 points from baseline to the later follow-up period. For the cohort of 72 patients, 69% reported improvement, 17% failed, and 12.5% reported no change from baseline to follow-up.

Minas et al prospectively followed 210 ACI-treated patients (362 grafts) for at least 10 years. Malalignment, patellar maltracking, and meniscal or ligamentous deficiency had also been corrected as needed. At a mean of 12 years of follow-up, 53 patients (25%) had graft failure. Nineteen of these patients (9%) went on to arthroplasty, 27 patients (13%) were salvaged with revision cartilage repair, and 7 patients declined further treatment. For the 157 patients who had successful grafts, functional outcomes were significantly improved from baseline to follow-up, as measured by the Western Ontario and McMaster Universities Index (WOMAC), Knee Society Score (KSS) for knee and function, and SF-36 (all p<0.001). Survival of the graft was significantly higher in patients with complex versus salvage-type lesions (p=0.03), with concomitant high tibial osteotomy (HTO) versus no HTO (p=0.01), and with primary ACI versus ACI after a prior marrow stimulation procedure (p=0.004). For example, ACI graft survival was 79% compared with 44% for knees with defects previously treated with microfracture.

In 2010, Peterson et al reported on 224 patients who replied to questionnaires at 10- to 20-year follow-up. This represents 38% of a total of 590 patients who underwent ACI at their institution between 1987 and 1998. Patients’ average age was 33 years (range, 14-61 years) at the time of the ACI, and the indication for treatment was any symptomatic full-thickness cartilage lesion up to 16 cm2, including meniscal (34% of patients) or ACL lesions (19%). Fifty-five patients (25%) had multiple lesions, 73 patients (33%) had unipolar or bipolar patellar lesions, and 26 patients (12%) had osteochondritis dissecans. Three hundred forty-one surveys were mailed to the treated patients; the response rate was 65%. Information about baseline measurements, collected from patients’ charts or from prior studies and when available, was compared with the questionnaire responses at follow-up. At a mean of 12.8 years of follow-
up, 74% of the patients reported their status as better or the same as the previous years, and 92% were satisfied with the surgery. The average LKSS score improved from 60.3 preoperatively to 69.5 postoperatively, Tegner from 7.2 to 8.2, and the Brittberg-Peterson from 59.4 to 40.9. At the final measurement, the KOOS score averaged 74.8 for pain, 63 for symptoms, 81 for activities of daily living, 41.5 for sports, and 49.3 for quality of life. The average Noyes score was 5.4. Patients with bipolar lesions had a worse final outcome than patients with multiple unipolar lesions. The presence of meniscal injuries before ACI or history of bone marrow procedures before the implantation did not seem to affect the final outcomes.

Rosenberger et al reported on an average 4.7-year follow-up (range, 2-11 years) for a cohort of 56 patients (45-60 years old) with lesions of the femoral condyle (49%), trochlea (29%), or patella (22%). Results were generally similar to those observed in younger patients, with 72% rating themselves as good or excellent, but 43% requiring additional arthroscopic procedures for periosteal-related problems and adhesion. A European group reported complications in 309 consecutive patients, 52 of whom (17%) had undergone revision surgery for persistent clinical problems. Three different ACI techniques had been used, periosteum-covered, membrane-covered (Chondro-Gide; Geistlich Biomaterials, Switzerland), and 3-dimensional matrix (BioSeed-C; BioTissue Technologies, Germany). Follow-up at a mean of 4.5 years showed that the highest rate of revision surgery was in patients with periosteum-covered ACI (27%) compared with membrane-covered or matrix-induced ACI (12% and 15%, respectively). There was a trend (p=0.09) for a higher incidence of hypertrophy with patellar defects than with the femoral condyles or trochlea.

ACI for patellar cartilage defects is typically reported as less effective than ACI for lesions of the femoral condyles, and some studies have reported biomechanical alignment procedures and unloading to improve outcomes for retropatellar ACI. In 2013, Trinh et al reported a systematic review of ACI combined with patellofemoral osteotomy (anteriorization and/or medialization) versus ACI alone. Eleven studies (10 level III or IV evidence) with a total of 366 patients were included. Three studies directly compared isolated ACI and combined treatment for patellar or trochlear lesions, showing a statistically significant benefit for the combined treatment.

In 2014, Biant et al reported a prospective study of long-term follow-up after ACI for large cartilage defects of knee, including lesions of the patella. Of 104 total procedures, 36 were performed on the patella. Seventy percent of patients had undergone a prior surgical procedure. Clinicians who were independent of the original surgery conducted the assessments at 10- to 12-year follow-up and were able to contact 100 patients. In the group as a whole, 26% experienced graft failure at a mean of 5.7 years after ACI. The percentage of failures in the subgroup with ACI of the patella was similar; 25% experienced graft failure at a mean of 5.8 years after ACI. Of the 32 patients who had not undergone a prior surgery, 6 (19%) had failed, compared with 21 of 72 (29%) who had a prior cartilage repair procedure, supporting other studies that have shown poorer outcomes for lesions with a failed prior surgical procedure.

In 2014, Gomoll et al reported a multicenter registry study of the treatment of mono- or bipolar patellar defects with ACI in 110 patients with a minimum of 4 year follow-up (mean, 90 months; range, 48-192 months). Concurrent surgical procedures included tibial tubercle osteotomy in 69% of patients, lateral release in 41%, vastus medialis advancement in 20%, and
trochleoplasty in 5%. At the latest follow-up, statistically and clinically significant improvements in pain and function were obtained on the IKDC, CKRS, WOMAC, and KSS, although it was noted that results were inferior to ACI for cartilage lesions of the femoral condyles. Excluding repeat arthroscopy for graft hypertrophy or lysis of adhesions, 9 patients were considered treatment failures.

Pascual-Garrido et al reported outcomes from 52 patients (83% follow-up) who underwent ACI of the patellofemoral joint (patella or trochlea). In addition to ACI of the patella, 67% of patients had concomitant procedures performed, including anteromedialization (n=28), lateral release (n=4), lateral meniscal transplant (n=2), and OA (n=1). Questionnaires were administered preoperatively, 6 months, and 1 year postoperatively, and then annually. At an average follow-up of 4 years (range, 2-7 years), there was significant improvement in the LKSS, IKDC, KOOS Pain, KOOS Symptoms, KOOS Activities of Daily Living, KOOS Sport, CKRS, Tegner, and SF-12 Physical Component Summary score. Patients reported the overall condition of their knee as excellent, very good, or good in 71% of the cases. There were 4 failures (8%), defined as poor clinical outcome accompanied by evidence of graft failure or need for conversion to knee arthroplasty or OA. A 2008 study from Europe described clinical results from 70 of 95 patients (74%) treated with ACI or matrix-induced ACI (MACI) for full-thickness defects of the patella.

Objective evaluation performed by an independent examiner who was blinded to data obtained at the time of surgery showed normal or nearly normal results in 47 patients (67%) at an average follow-up of 38 months. Other studies from Europe report patellofemoral cartilage defects treated with second-generation MACI implants. These products are not approved in the United States and are, therefore, considered investigational.

Farr et al described outcomes from a prospective series of 36 patients who underwent ACI together with meniscal transplantation in the same compartment. Lesions ranged from 1.5 to 12.1 cm². Patients identified with advanced chondrosis during staging arthroscopy were excluded from the study. Four patients received treatment for bipolar lesions, while 16 of the procedures were done concomitant with another procedure such as osteotomy, patellar realignment, or ACL reconstruction. Four patients (11%) were considered failures before 2 years, and 3 were lost to follow-up (8%), resulting in 29 evaluable patients at an average of 4.5 years after surgery. The LKSS score improved from an average of 58 to 78; maximum pain decreased an average 33% (from 7.6 to 5.1). Excluding the 4 failures, 68% of the patients required additional surgeries; 52% had 1 additional surgery, and 16% required 2 or more additional surgeries. The most common procedures were trimming of periosteal overgrowth or degenerative rims of the transplanted meniscus. Another report described average 3.1 years of follow-up from a prospective series of 30 patients (31 procedures) who had undergone combined meniscal allograft transplantation with ACI (52%) or OA transplantation (48%). The LKSS score improved in both the ACI (from 55 to 79) and OA (from 42 to 68) groups; 48% of patients (60% ACI, 36% OA) were considered to be normal or nearly normal at the latest follow-up. Patients treated with OA were on average older (average, 37 years vs 23 years) and had larger lesions (5.5 cm² vs 3.9 cm²). Two patients were considered failures (7%) and 5 (17%) and underwent subsequent surgery. Although results seemed promising, evidence is insufficient to permit conclusions regarding the effect of combined transplantation-implantation procedures on health outcomes.
A 3-fold increased failure of ACI after previous treatment with marrow stimulation techniques was found in a cohort of 321 patients with more than 2 years of follow-up (of 332 treated). The average lesion was 8 cm², and the indications for treatment of cartilage defects with ACI included 1 or more full-thickness chondral defects of the knee, with consistent history, physical examination, imaging, and arthroscopy; no or correctable ligamentous instability, malalignment, or meniscal deficiency; and not more than 50% loss of joint space on weight-bearing radiographs. Independent analysis showed a failure rate of 8% of joints (17/214) that did not have prior marrow stimulation of the lesion, compared with 26% (29/111 joints) that had previously been treated with marrow stimulation. A study of 1000 patients treated with ACI or MACI found that overall graft survival was 78.2% at 5 years and 50.7% at 10 years by Kaplan-Meier analysis, with no significant difference in survival rates between ACI and MACI procedures or for different defect sizes (range, 0.64-20.75 cm²). Graft failure was 5 times more likely with a previously treated lesion (<25% survival at 12 years) compared with a previously untreated lesion (>75% survival at 12 years). Survival of grafts in the lateral femoral condyle was superior to grafts in the medial femoral condyles, trochlea, or patella.

Minas et al assessed the influence of ACI on the need for joint replacement surgery in 153 patients (155 knees) with a mean age of 38 years (range, 17-60 years), evidence of early OA at the time of surgery (peripheral intra-articular osteophyte formation and/or 0%-50% joint space narrowing), and 2 years or more of follow-up. (Patients with >50% loss of joint space were ineligible for treatment with ACI.) Patients were also included if they had normal radiographs but evidence of bipolar lesions or generalized chondromalacia noted at the time of surgery. An average of 2.1 defects per knee was treated, with a mean defect size of 4.9 cm² and a total mean defect area of 10.4 cm². Defects were located on the femoral condyle (n=150), trochlea (n=85), patella (n=60), and tibial plateau (n=14). There were 42 (27%) bipolar lesions, most of which were patellofemoral. Concurrent procedures included correction of tibiofemoral malalignment (31% of knees) and patellar maltracking (28% of knees). At 5 years postoperatively (range, 24-132 months), 12 knees (8%) were considered treatment failures and underwent arthroplasty due to graft failure (n=3), inadequate pain relief (n=1), and progression of osteoarthritic disease beyond the originally transplanted defect area (n=8). The remaining 92% of patients showed improvements in all scores from baseline to final follow-up. For example, there was 52% improvement in WOMAC subscales, and the proportion of patients who experienced severe or extreme pain while walking on a flat surface decreased by 73%. Subsequent surgical procedures after the index implantation were performed in 95 knees (61%), including 52 cases of periosteal hypertrophy, 32 cases of arthrofibrosis, 23 graft complications, and 11 for periosteal delamination.

First-Generation ACI (Carticel™) for Joints Other Than the Knee
There has been interest in applying ACI to cartilage defects in other joints. The most commonly reported is use of ACI for the talus.

In 2010, Zengerink et al published a systematic review of treatment of osteochondral lesions of the talus. Fifty-one nonrandomized and 1 randomized trials were included in the review. Success rates were 85% for bone marrow stimulation, 87% for osteochondral autografting, and 76% for ACI. Because of the high cost of ACI and the knee morbidity seen with osteochondral autografting, the authors concluded that bone marrow stimulation is the treatment of choice for primary osteochondral talar lesions. A 2009 report examined the association between defect size and outcomes following marrow stimulation techniques in 120 ankles. Eight ankles subsequently underwent osteochondral transplantation, and 22 ankles were considered clinical
failures (American Orthopaedic Foot and Ankle Society [AOFAS] Ankle-Hindfoot Score <80). Linear regression suggested a cutoff defect size of 1.5 cm2 for marrow stimulation techniques, with an 80% failure rate compared with a 10.5% failure rate for ankles with a defect size of less than 1.5 cm2. Three of 58 ankles (5.2%) with a defect area of less than 1 cm2 showed clinical failure, while 7 of 37 ankles (18.9%) with a defect area between 1.0 and 1.5 cm2 failed.

A systematic review by Niemeyer et al included 16 studies (213 patients) on ACI or MACI for lesions of the talus. All were case series with a mean sample of 13 patients (range, 2-46 patients) and mean follow-up of 32 months (range, 6-120 months). Most studies were prospective. In 6 studies, periosteum-covered ACI was applied while 10 studies used second-generation MACI. MACI uses a matrix seeded with cultured autologous chondrocytes, and, unlike first-generation ACI, does not require tibial or fibular osteotomy to gain adequate surgical access. For the studies using periosteum-covered ACI, the number of subjects ranged from 4 to 12. Nine different methods were used to evaluate pre- and postoperative clinical function, with the most common being the AOFAS Ankle-Hindfoot Score. Overall clinical success rate, defined as the percentage of good and excellent results, was 89.9% (range, 50%-100%). Interpretation of these results is limited by the inclusion of poor quality studies, lack of comparators, lack of blinding, and use of techniques not approved for use by the U.S. Food and Drug Administration (FDA).

Second-Generation ACI Products

Systematic Review
Kon et al published a systematic review of MACI in 2013. The review identified 51 articles, including 3 RCTs, 10 comparative studies, 33 case series, and 5 case reports that reported on functional or clinical outcomes. The review found an expanding evidence base of good results at short to medium follow-up, although long-term follow-up and RCTs are needed to compare MACI with other available treatments.

Randomized Controlled Trials
There are 5 RCTs of MACI. Four of these compared MACI with marrow-stimulating techniques, and the third RCT compared MACI with ACI.

MACI®
SUMMIT was an industry-sponsored multicenter randomized open-label trial (NCT00719576) comparing MACI® with microfracture for larger cartilage defects (≥3 cm2), which typically fare worse than smaller lesions when treated with microfracture. Patients (N=144) were included who had at least 1 symptomatic grade III or IV focal cartilage defect on the femoral condyles or trochlea, a stable knee, an intact or partial meniscus, and a moderate-to-severe KOOS Pain value (<55). Average lesion size was 4.8 cm2 (range, 3-20 cm2); 34.6% of patients had undergone a prior marrow stimulation procedure. At 2-year follow-up, the MACI® group had significantly better subscores for KOOS Pain (coprimary outcome, difference of 11.76, p<0.001) and Function (coprimary outcome; difference, 11.41; p=0.16) as well as the other KOOS subscales (Activities of Daily Living, Knee-Related Quality of Life, Other Symptoms). With response to treatment defined as a 10-point improvement in both the KOOS Pain and Function subscales, significantly more patients in the MACI group responded to treatment than in the microfracture group (87.5% vs 68.1%, p=0.016). There were no significant differences between the groups for cartilage repair, as measured by second look arthroscopy, biopsy, or
magnetic resonance imaging (MRI). The lack of blinding in this study reduced the validity of the patient-reported outcome measures.

Basad et al reported a small randomized trial that compared MACI® (n=40) with microfracture (n=20) in patients with a single posttraumatic chondral defect between 4 and 10 cm². Both groups improved at the 2-year follow-up, with a significant advantage of MACI over microfracture on the LKSS (92 vs 69), Tegner (4 vs 3), and International Cartilage Repair Society (ICRS) patient (a higher percentage of patients with an ICRS score of 1) and ICRS surgeon scores.

Neocart
In 2012, Crawford et al reported results of an industry-sponsored, FDA-regulated, multicenter randomized phase 2 trial. Thirty patients with lesions less than 8 cm² were randomized to Neocart (n=21) or to microfracture (n=9). The SF-36, KOOS, IKDC, and visual analog scale (VAS) pain scores were assessed at up to 24 months by intention-to-treat analysis, and patients were classified as responders if they had at least a 12-point improvement in the Pain score of the KOOS and a 20-point improvement in the IKDC subjective score. At 24 months, there was no significant difference in the mean KOOS Pain scores or IKDC scores. The Neocart group showed significantly greater improvement in the KOOS Pain score, KOOS Sports, KOOS knee-related quality of life, IKCD, and VAS pain scores compared with microfracture. There was a trend for a greater number of responders in the Neocart group (p=0.097); 79% of Neocart patients were considered to be responders compared with 44% of the microfracture group.

Bioseed
Zeifang et al conducted a small (N=21) randomized trial comparing MACI and ACI. The average size of the cartilage defects was 4.3 cm², and patients had undergone an average of 2 prior surgeries on the affected knee. Postoperatively, there was no significant difference between the 2 groups on the IKDC score at either 12 months (72.0 for MACI, 76.7 for ACI) or at 24 months (70.1 for MACI, 77.1 for ACI). Exploratory analysis found a significant inverse correlation with age (r = -0.52 at 12 months, r = -0.49 at 24 months) indicating that better results were observed in younger patients. There was no significant difference between the groups in the SF-36. The LKSS score showed a significant improvement only in the ACI group (from 61.3 at baseline to 86.3 at 12 months to 84.0 at 24 months). The Tegner activity score did not change significantly in either group.

ChondroCelect
Saris et al published a multicenter, randomized trial of characterized chondrocyte implantation (n=57) versus microfracture (n=61) in 2008; the average lesion size was 2.8 cm². Chondrocytes were isolated from a cartilage biopsy specimen and expanded ex vivo (ChondroCelect; TiGenix, Belgium). ChondroCelect is not approved for use in the United States. Chondrocytes that were predicted to form stable hyaline cartilage in vivo were implanted by arthroscopy approximately 27 days after chondrocyte harvest. Surgical and rehabilitation procedures were standardized, and evaluation of a biopsy specimen at 12 months was conducted by an independent evaluator. Histologic analysis showed better results with ACI for some measures of structural repair such as cartilage surface area, safranin O and collagen II ratio, and cell morphology. However, measures of integration (eg, subchondral bone abnormalities, basal integration, vascularization) and surface architecture did not
improve relative to the microfracture group. Self-assessed pain and function with the KOOS questionnaire were similar following ACI or microfracture at 12 or 18 months of follow-up. Joint swelling and joint crepitation were greater in the ACI group, particularly following the arthroscopy. Thus, although histologic results were somewhat improved, in this study, characterized chondrocyte implantation did not improve health outcomes compared with microfracture at short-term follow-up.

In 2009, Saris et al published 36-month outcomes (100% follow-up) from this randomized trial. Mean improvement in the overall KOOS was greater in the ACI group than in the microfracture group (21 points vs 16 points, respectively). More ACI than microfracture-treated patients were considered treatment responders (83% vs 62%, respectively), defined as an increase from baseline of at least 10 percentage points on at least 3 of the 4 KOOS subdomains or a decrease of at least 20 percentage points in VAS scores for pain. At 36 months postsurgery, 2 ACI (3.9%) and 7 microfracture patients (11.5%) had failed treatment and subsequently underwent reintervention. MRI showed greater worsening of the subchondral bone reaction with microfracture compared with ACI. At 5 years after treatment, the number of treatment failures was comparable for the ACI (n=7) and microfracture (n=10) groups. There was a trend for greater improvement in overall KOOS score following ACI than microfracture (21 vs 14, p=0.068). Planned exploratory subgroup analysis indicated that ACI resulted in a better outcome (both statistically and clinically significant) in patients who had a time since symptom onset of less than 3 years, with a change in KOOS of 26 (vs 15 for the microfracture group). For patients with symptom onset of 3 years or more, the change in KOOS was similar for the 2 groups (13 ACI vs 17 microfracture). Subgroup analyses for age did not show a difference for patients who were younger than 35 years of age compared with patients who were older than 35 years.

**Hyalograft C**

In 2011, Kon et al reported a prospective comparative study of second-generation ACI (Hyalograft C) versus microfracture in 41 professional or semiprofessional male soccer players. This was a pragmatic clinical trial, with treatment allocation based on the center patients chose; 1 center performed ACI and 2 centers performed microfracture. The 2 patient groups were comparable for age, defect size, location, previous and combined surgery, and follow-up. Patients were evaluated prospectively at 2 years and at a final mean 7.5-year follow-up (minimum, 4 years). The percentage of patients who returned to competition was similar, with 80% in the microfracture group and 86% in the ACI group. Patients treated with microfracture needed a median of 8 months before playing their first official soccer game, whereas the ACI group required a median time of 12.5 months. The IKDC subjective score showed similar results at 2-year follow-up but significantly better results in the ACI group at the final evaluation. In the microfracture group, results decreased over time (from 86.8 at 2 years to 79.0 at final follow-up), whereas the ACI group had stable results between 2 years and final follow-up (90.5 and 91.0, respectively). The IKDC objective score was similar in the 2 groups, with 90% to 95% of knees considered to be normal or nearly normal. Subjective evaluation of functional level was significantly better in the ACI group at final follow-up (91 vs 84).

In 2014, the same group of investigators compared outcomes following repair of trochlear or patellar lesions with Hyalograft C. Other procedures conducted at the same time included lateral release, realignment, meniscectomy, ACL reconstruction, or trochleoplasty. Patients were followed for 5 years and evaluated every year with the IKDC subjective score, EuroQoL
VAS, Kujala score, and Tegner score. Failure was defined as the need for further surgery because of symptoms related to the primary defect. Both cohorts showed significant improvements in outcomes, and patients with trochlear lesions improved more than patients with patellar lesions, although neither group reached the preinjury level.

Summary of Evidence
The evidence for autologous chondrocyte implantation (ACI) for individuals who have focal articular cartilage lesions of the knee includes randomized controlled trials (RCTs) and prospective observational studies. Relevant outcomes are symptoms, functional outcomes, implant survival, quality of life, and resource utilization. Although evidence from long-term studies is still accumulating, current evidence indicates that Food and Drug Administration–approved ACI products can improve symptoms in some patients with lesions of the articular cartilage of the knee. These patients, who are too young for total knee replacement, have limited options. Therefore, ACI may be considered an option for large disabling full-thickness chondral lesions of the knee caused by acute or repetitive trauma. Evidence indicates that a prior surgical procedure may negatively impact the success of ACI, but ACI combined with meniscal allograft results in outcomes similar to either procedure performed alone. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence on ACI for individual who have focal articular cartilage lesions in joints other than the knee is limited. Relevant outcomes are symptoms, functional outcomes, implant survival, quality of life, and resource utilization. The greatest amount of literature is for ACI of the talus. A systematic review found that outcomes following treatment with ACI were inferior to microfracture. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2015 Input
In response to requests regarding the use of ACI for patellar lesions, input was received from 2 physician specialty societies (6 reviewers) and 4 academic medical centers while this policy was under review in 2015. The clinical input was generally supportive of the use of ACI for large patellar lesions, although there was a range in the degree of support. Reviewers indicated that outcomes were improved when realignment procedures were performed concurrently with ACI of the patella, and that success rates were lower when using ACI after a prior microfracture. A majority of reviewers recommended that a prior surgical procedure not be required for lesions greater than 4 cm2.

2011 Input
In response to requests, input was received from 2 physician specialty societies and 3 academic medical centers while this policy was under review in 2011. The clinical input was generally in agreement with the stated criteria for ACI with the exception of the following: input was mixed regarding the requirement for an inadequate response to a prior surgical procedure and the requirement for an absence of meniscal pathology. Input was also mixed regarding the investigational status of ACI in patellar and talar joints.

2008 Input
In response to requests, input was received from 1 physician specialty society and 3 academic medical centers while this policy was under review in 2008. The reviewers generally agreed that ACI should be considered when all other treatments have been unsuccessfully tried in patients who have a localized chondral defect in an otherwise normal joint articular surface. Reviewers noted the lack of alternative options for larger lesions (eg, >4 cm2). Additional literature was provided, which was subsequently reviewed.

Practice Guidelines and Position Statements

American Academy of Orthopaedic Surgeons
In a 2010 clinical practice guideline on the diagnosis and treatment of osteochondritis dissecans (OCD), the American Academy of Orthopaedic Surgeons was unable to recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable OCD lesion. This recommendation of insufficient evidence was based on a systematic review that found 4 level IV studies that addressed cartilage repair techniques for an unsalvageable OCD lesion. Because each of the level IV articles used different techniques, different outcome measures, and differing lengths of follow-up, the work group deemed that the evidence for any specific technique was inconclusive.

National Institute for Health and Clinical Excellence
In 2005, the National Institute for Health and Clinical Excellence (NICE) issued an updated Technology Appraisal Guidance on the use of ACI. The NICE guidance cited insufficient evidence to determine the benefits of ACI and indicated this technology “should not be used for the treatment of articular cartilage defects except where the treatment is part of a clinical study.” The guidance noted many limitations in available trial data including length of follow-up, comparison with conservative treatment, assessment of the quality of cartilage produced, and the impact of cartilage produced on functional outcomes and health-related quality of life.

Reference Resources


Document Precedence

Blue Cross and Blue Shield of Vermont (BCBSVT) Medical Policies are developed to provide clinical guidance and are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. The applicable group/individual contract and member certificate language, or employer’s benefit plan if an ASO group, determines benefits that are in effect at the time of service. Since medical practices and knowledge are constantly evolving, BCBSVT reserves the right to review and revise its medical policies periodically. To the extent that there may be any conflict between medical policy and contract/employer benefit plan language, the member’s contract/employer benefit plan language takes precedence.

Audit Information

BCBSVT reserves the right to conduct audits on any provider and/or facility to ensure compliance with the guidelines stated in the medical policy. If an audit identifies instances of non-compliance with this medical policy, BCBSVT reserves the right to recoup all non-compliant payments.

Administrative and Contractual Guidance

Benefit Determination Guidance

Prior approval is required and benefits are subject to all terms, limitations and conditions of the subscriber contract.

Incomplete authorization requests may result in a delay of decision pending submission of missing information. To be considered compete, see policy guidelines above.
An approved referral authorization for members of the New England Health Plan (NEHP) is required. A prior approval for Access Blue New England (ABNE) members is required. NEHP/ABNE members may have different benefits for services listed in this policy. To confirm benefits, please contact the customer service department at the member’s health plan.

Federal Employee Program (FEP): Members may have different benefits that apply. For further information please contact FEP customer service or refer to the FEP Service Benefit Plan Brochure. It is important to verify the member’s benefits prior to providing the service to determine if benefits are available or if there is a specific exclusion in the member’s benefit.

Coverage varies according to the member’s group or individual contract. Not all groups are required to follow the Vermont legislative mandates. Member Contract language takes precedence over medical policy when there is a conflict.

If the member receives benefits through an Administrative Services Only (ASO) group, benefits may vary or not apply. To verify benefit information, please refer to the member’s employer benefit plan documents or contact the customer service department. Language in the employer benefit plan documents takes precedence over medical policy when there is a conflict.

Policy Implementation/Update information

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<tr>
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<td>05/2011</td>
<td>Minor updates</td>
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<td>02/2014</td>
<td>ICD-10 remediation only, RLG</td>
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<tr>
<td>04/2017</td>
<td>Updated to align with BCBSA MPRM 7.01.48. Updated references. Formatting changes. Removed ICD 9-PCS &amp; ICD10-PCS Tables. Updated ICD 10 table with new codes.</td>
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Eligible providers

Qualified healthcare professionals practicing within the scope of their license(s).

Approved by BCBSVT Medical Directors Date Approved

Gabrielle Bercy-Roberson, MD, MPH, MBA
Senior Medical Director
Chair, Health Policy Committee
### ATTACHMENT I
#### CPT Code Table & Instructions

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<tr>
<th>Code Type</th>
<th>Number</th>
<th>Description</th>
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<td>Autologous chondrocyte implantation, knee</td>
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<td>Arthroscopy, knee, surgical for harvesting of cartilage (chondrocyte cells)</td>
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### ATTACHMENT II
#### ICD-10 Diagnosis code table

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<td>M25.369</td>
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<td>Other internal derangements of unspecified knee</td>
<td>S89.90XA</td>
<td>Unspecified injury of unspecified lower leg, initial encounter</td>
</tr>
<tr>
<td>M25.161</td>
<td>Fistula, right knee</td>
<td>S89.90XD</td>
<td>Unspecified injury of unspecified lower leg, subsequent encounter</td>
</tr>
<tr>
<td>M25.162</td>
<td>Fistula, left knee</td>
<td>S89.90XS</td>
<td>Unspecified injury of unspecified lower leg, sequela</td>
</tr>
<tr>
<td>M25.169</td>
<td>Fistula, unspecified knee</td>
<td>S89.91XA</td>
<td>Unspecified injury of right lower leg, initial encounter</td>
</tr>
<tr>
<td>M25.261</td>
<td>Flail joint, right knee</td>
<td>S89.91XD</td>
<td>Unspecified injury of right lower leg, subsequent encounter</td>
</tr>
<tr>
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<td>Flail joint, left knee</td>
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</tr>
<tr>
<td>M25.269</td>
<td>Flail joint, unspecified knee</td>
<td>S89.92XA</td>
<td>Unspecified injury of left lower leg, initial encounter</td>
</tr>
<tr>
<td>M25.361</td>
<td>Other instability, right knee</td>
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<td>Unspecified injury of left lower leg, subsequent encounter</td>
</tr>
<tr>
<td>M25.362</td>
<td>Other instability, left knee</td>
<td>S89.92XS</td>
<td>Unspecified injury of left lower leg, sequela</td>
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