BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions

Policy #: 156
Latest Review Date: April 2023
Category: Surgery

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat **autologous chondrocyte implantation** as a **covered benefit** for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma, when all of the following criteria are met:

- The patient is skeletally mature with documented closure of growth plates and not considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., age greater than 15 and less than 55 years); AND
- Focal, full-thickness (grade III or IV) unipolar lesions of the patella or the weight-bearing surface of the femoral condyles or trochlea at least 1.5 cm^2 in size; AND
- 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; AND
- Normal knee biomechanics or alignment and stability achieved concurrently with autologous chondrocyte implantation.

Blue Advantage will treat **autologous chondrocyte implantation** as a **non-covered benefit** and as **investigational** for all other joints, including talar, and any indications other than those listed above is therefore considered investigational.

Blue Advantage will treat **prophylactic harvesting of cells during other reconstructive or reparative procedures** for possible future implantation as a **non-covered** benefit and as **investigational**.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

A variety of procedures are being developed to resurface articular cartilage defects. Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral defect under a periosteal or fibrin patch. Second- and third- generation techniques include combinations of autologous chondrocytes, scaffolds, and growth factors. This procedure may be performed at the same time as other surgical procedures such as repair of tendons or ligaments, osteotomies for realignment of a joint, or meniscal allograft transplantation.

Damaged articular cartilage typically fails to heal on its own and can be associated with pain, loss of function, and disability, and may lead to debilitating osteoarthritis over time. These

manifestations can severely impair an individual's activities of daily living and adversely affect the quality of life.

Conventional treatment options include debridement, subchondral drilling, microfracture, and abrasion arthroplasty. Debridement involves the removal of synovial membrane, osteophytes, loose articular debris, and diseased cartilage and is capable of producing symptomatic relief. Subchondral drilling, microfracture, and abrasion arthroplasty attempt to restore the articular surface by inducing the growth of fibrocartilage into the chondral defect. Compared with the original hyaline cartilage, fibrocartilage has less capability to withstand shock or shearing force and can degenerate over time, often resulting in the return of clinical symptoms. Osteochondral grafts and autologous chondrocyte implantation (ACI) attempt to regenerate hyaline-like cartilage and thereby restore durable function. Osteochondral grafts for the treatment of articular cartilage defects are discussed in Medical Policy #248, Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions.

With ACI, a region of healthy articular cartilage is identified and biopsied through arthroscopy. The tissue is sent to a facility licensed by the U.S. Food and Drug Administration (FDA) where it is minced and enzymatically digested, and the chondrocytes are separated by filtration. The isolated chondrocytes are cultured for 11 to 21 days to expand the cell population, tested, and then shipped back for implantation. With the patient under general anesthesia, an arthrotomy is performed, and the chondral lesion is excised up to the normal surrounding cartilage. Methods to improve the first-generation ACI procedure have been developed, including the use of a scaffold or matrix-induced autologous chondrocyte implantation (MACI) composed of biocompatible carbohydrates, protein polymers, or synthetics. The only FDA-approved MACI product to date is supplied in a sheet, which is cut to size and fixed with fibrin glue. This procedure is considered technically easier and less time consuming than the first-generation technique, which required suturing of a periosteal or collagen patch and injection of chondrocytes under the patch.

Desired features of articular cartilage repair procedures are the ability (1) to be implanted easily, (2) to reduce surgical morbidity, (3) not to require harvesting of other tissues, (4) to enhance cell proliferation and maturation, (5) to maintain the phenotype, and (6) to integrate with the surrounding articular tissue. In addition to the potential to improve the formation and distribution of hyaline cartilage, use of a scaffold with MACI eliminates the need for harvesting and suture of a periosteal or collagen patch. A scaffold without cells may also support chondrocyte growth.

KEY POINTS:

The most recent literature update was performed through February 16, 2023.

Summary of Evidence

For individuals who have focal articular cartilage lesion(s) of the weight-bearing surface of the femoral condyles, trochlea, or patella who receive ACI, the evidence includes systematic reviews, randomized controlled trials, and observational studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, and quality of life. There is a large body of evidence on ACI for the treatment of focal articular cartilage lesions of

the knee. For large lesions, ACI results in better outcomes than microfracture, particularly in the long term. In addition, there is a limit to the size of lesions that can be treated with osteochondral autograft transfer, due to a limit on the number of osteochondral cores that can be safely harvested. As a result, ACI has become the established treatment for large articular cartilage lesions in the knee. In 2017, first-generation ACI with a collagen cover was phased out and replaced with an ACI preparation that seeds the chondrocytes onto a bioresorbable collagen sponge. Although the implantation procedure for this second-generation ACI is less technically demanding, studies to date have not shown improved outcomes compared with first-generation ACI. Some evidence has suggested an increase in hypertrophy (overgrowth) of the new implant that may exceed that of the collagen membrane covered implant. Long-term studies with a larger number of patients will be needed to determine whether this hypertrophy impacts graft survival. Based on mid-term outcomes that approximate those of first-generation ACI and the lack of alternatives, secondgeneration ACI may be considered an option for large disabling full-thickness cartilage lesions of the knee. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have focal articular cartilage lesions of joints other than the knee who receive autologous chondrocyte implantation, the evidence includes case series, systematic reviews of case series, and a network meta-analysis of prospective(none of which evaluated autologous chondrocyte implantation) and retrospective studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, and quality of life. The greatest amount of literature is for ACI of the talus. Comparative trials are needed to determine whether ACI improves outcomes for lesions in joints other than the knee. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
American Academy of Orthopaedic Surgeons
In its 2010 guidelines 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. This recommendation of insufficient evidence was based on a systematic review that found four level IV studies that addressed cartilage repair techniques for an unsalvageable OCD lesion. Since each of the level IV articles utilized 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 2018, the National Institute for Health and Care Excellence updated its 2005 guidance on the use of autologous chondrocyte implantation. The NICE recommendations are stated below:

"… as an option for treating symptomatic articular cartilage defects of the femoral condyle and patella of the knee (International Cartilage Repair Society grade III or IV) in adults, only if:

- the person has not had previous surgery to repair articular cartilage defects;

- there is minimal osteoarthritic damage to the knee (as assessed by clinicians experienced in investigating knee cartilage damage using a validated measure for knee osteoarthritis); and
- the defect is over 2 cm^2."

U.S. Preventive Services Task Force Recommendations
Not applicable.

KEY WORDS:
Autologous chondrocyte transplantation (ACT), autologous chondrocyte implant (ACI), articular cartilage, chondrocytes, Carticel®, osteochrondritis dissecans (OCD), ChondroCelect, BioCart II, Cartilix, MACI®, Cartipatch, NeoCart, Hyalograft C

APPROVED BY GOVERNING BODIES:
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. 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.…"

In 2016, MACI® (matrix-induced autologous chondrocyte implantation [ACI]; Vericel), received FDA approval for the repair of symptomatic, full-thickness cartilage defects of the knee in adult patients. MACI® consists of autologous chondrocytes which are cultured onto a bio-resorbable porcine-derived collagen membrane. In 2017, production of Carticel was phased out and MACI® is the only ACI product that is available in the U.S.

A number of other second-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development or testing or are available outside of the United States. They include Atelocollagen (Koken), a collagen gel; Bioseed® C (BioTissue Technologies), a polymer scaffold; CaReS (Ars Arthro), collagen gel; Cartilix (Biomet), a polymer hydrogel; Chondron (Sewon Cellontech), a fibrin gel; Hyalograft C (Fidia Advanced Polymers), a hyaluronic acid-based scaffold; NeoCart (Histogenics), an ACI with a 3-dimensional chondromatrix in a phase 3 trial; and Novocart®3D (Aesculap Biologics), a collagenchondroitin sulfate scaffold in a phase 3 trial. ChondroCelect® (TiGenix), characterized as a chondrocyte implantation with a completed phase 3 trial, uses a gene marker profile to determine in vivo cartilage-forming potential and thereby optimizes the phenotype (e.g., 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. Both Hyalograft C and ChondroCelect® have been withdrawn from the market in Europe. In 2020, the FDA granted breakthrough status to Agili-C (CartiHeal, Ltd.), a proprietary cell-free biocompatible and biodegradable tapered-shape implant for the treatment of cartilage lesions in arthritic and non-arthritic joints that, when implanted into a pre-prepared osteochondral hole, acts as a 3D scaffold that potentially supports

and promotes the regeneration of the articular cartilage and its underlying subchondral bone. Agili-C was FDA-approved in 2021 for treatment of knee-joint surface lesions with a treatable area of 1 to 7 cm^2 without severe osteoarthritis.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT codes:

27412	Autologous chondrocyte implantation, knee
27899	Unlisted procedure, leg or ankle
29870-29887	Code range, arthroscopy of the knee

HCPCS:

J7330	Autologous cultured chondrocytes, implant
S2112	Arthroscopy, knee, surgical for harvesting of cartilage (chondrocyte cells)

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POLICY HISTORY:

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Medical Policy Group, December 2017
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Medical Policy Group, January 2021
Medical Policy Group, April 2021
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