Corporate Medical Policy

Autologous Chondrocyte Implantation

File Name: autologous_chondrocyte_implantation
Origination: 4/1996
Last Review: 6/2023

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 . Second and third generation techniques include combinations of autologous chondrocytes, scaffolds, and growth factors.

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 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 to 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 the BCBSNC policy titled, "Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions".

With autologous chondrocyte implantation, 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 11-21 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 composed of biocompatible carbohydrates, protein polymers, or synthetics. The only FDA-approved matrix-induced autologous chondrocyte implantation 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 matrix-induced autologous chondrocyte implantation

eliminates the need for harvesting and suture of a periosteal or collagen patch. A scaffold without cells may also support chondrocyte growth.

The culturing of chondrocytes is considered by the FDA to fall into the category of manipulated autologous structural cells, which are subject to a biologic licensing requirement. In 1997, Carticel® (Genzyme; now Vericel) 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 December 2016, MACI® (Vericel), received FDA approval for "the repair of symptomatic, single or multiple full-thickness cartilage defects of the knee with or without bone involvement in adults." MACI® consists of autologous chondrocytes that are cultured onto a bioresorbable porcine-derived collagen membrane. In 2017, production of Carticel® was phased out and MACI® is the only ACI product that is available in the United States.

A number of other second-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development/testing or are available only outside of the U.S. These 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 autologous chondrocyte implantation with a 3-dimensional chondromatrix in a phase 3 trial; and Novocart®3D (Aesculap Biologics), a collagen chondroitin sulfate scaffold in a phase 3 trial. ChondroCelect® (TiGenex) 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 autologous chondrocyte implantation 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 3-dimensional 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 cm2 without severe osteoarthritis.

Related Policies
Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions
Meniscal Allografts and Other Meniscal Implants
Orthopedic Applications of Stem Cell Therapy

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for Autologous Chondrocyte Implantation when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Autologous Chondrocyte Implantation

When Autologous Chondrocyte Implantation is covered

Autologous chondrocyte implantation may be considered medically necessary 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:

1. 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),

2. Focal, full thickness (grade III or IV) unipolar lesions of the weight bearing surface of the femoral condyles, trochlea, or patella at least 1.5 cm^2 in size,

3. 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,

4. Normal knee biomechanics, or alignment and stability achieved concurrently with autologous chondrocyte implantation.

When Autologous Chondrocyte Implantation is not covered

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

Autologous chondrocyte implantation is not covered for all other indications, including, but not limited to:

- Talar lesions,
- Patients who have an infection at any of the operative sites,
- Osteoarthritis,
- Inflammatory diseases of the joint,
- Patients with a known history of an allergy to the antibiotic gentamicin,
- Patients with sensitivities to materials of a bovine origin,
- Patients with an unstable knee,
- Patients who have abnormal distribution of weight within the joint,
- Patients who have had previous cancer in the bones, cartilage, fat, or muscle of the treated limb,
- Kissing lesions, and
- Total meniscectomy.

Policy Guidelines

For smaller lesions (e.g., smaller than 4 $cm^{2)}$, 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 $5cm^2$; many studies treated lesions as large as $15cm^2$.

Severe obesity (body mass index > 35 kg/m^2), 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. In addition, meniscal allograft transplantation may be performed in combination, either concurrently or sequentially, with autologous chondrocyte implantation. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

For individuals who have focal articular cartilage lesion(s) of the weight-bearing surface of the femoral condyles, trochlea, or patella who receive autologous chondrocyte implantation, the evidence includes systematic reviews, randomized controlled trials (RCTs), 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 autologous chondrocyte implantation for the treatment of focal articular cartilage lesions of the knee. For large lesions, autologous chondrocyte implantation 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, autologous chondrocyte implantation has become the established treatment for large articular cartilage lesions in the knee. In 2017, first-generation autologous chondrocyte implantation with a collagen cover was phased out and replaced with an autologous chondrocyte implantation preparation that seeds the chondrocytes onto a bioresorbable collagen sponge. Although the implantation procedure for this second-generation autologous chondrocyte implantation is less technically demanding, studies to date have not shown improved outcomes compared to first-generation autologous chondrocyte implantation. Some evidence has suggested 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 autologous chondrocyte implantation and the lack of alternatives, second-generation autologous chondrocyte implantation 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 an 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 autologous chondrocyte implantation of the talus. Comparative trials are needed to determine whether autologous chondrocyte implantation improves outcomes for lesions in joints other than the knee. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Autologous Chondrocyte Implantation

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J7330, S2112, 27412*

Arthrotomy and Arthroscopy procedure codes may be used - 29870, 29871, 29873, 29874, 29875, 29876, 29877, 29879, 29880, 29881, 29882, 29883, 29884, 29885, 29886, 29887, 27334, 27335, 27403.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

For Policy Titled: Autologous Chondrocyte Transplantation

TEC Bulletin - 3/96

BCBSA Medical Policy Reference Manual - 7/96

Consultant Review- 11/96

TEC Evaluation - 1997

TEC Evaluation - 2/98; Volume 12, Tab No. 26

BCBSA Medical Policy Reference Manual - 4/1/98

BCBSA Medical Policy Reference Manual - 7/10/98

CarticelTM (Autologous Cultured Chondrocytes) - Genzyme Tissue Repair Presentation - 2/24/99

Medical Policy Advisory Group - 5/99

1999 USPDI - 19th Edition, Volume 1; pps. 856-858.

Specialty Matched Consultant Advisory Panel - 9/2000

Medical Policy Advisory Group - 10/2000

Specialty Matched Consultant Advisory Panel - 8/2002

BCBSA TEC Assessment [Electronic Version]. June 2003.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 12/17/03.

ECRI Health Technology Assessment. (June 23, 2004). Autologous Chondrocyte Implantation for Knee Cartilage Defects.

Specialty Matched Consultant Advisory Panel - 7/2004

National Institute for Health and Clinical Excellence (NICE) Technology Appraisal Guidance 89. (May 2005). The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints. Retrieved April 3, 2006 from http://www.nice.org.uk/nicemedia/pdf/TA089guidance.pdf

ECRI Custom Hotline Response. (February 2006). Osteochondral Autograft Transplantation in the Knee.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 12/13/07

For Policy Renamed: Autologous Chondrocyte Implantation

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 11/13/08

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 3/11/2010

Food and Drug Administration (FDA). Approval letter for Carticel, August 27, 1997. Retrieved on May 7, 2010 from http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/ucm171702.htm

McCormick F, Yanke A, Provencher MT et al. Minced articular cartilage: basic science, surgical technique, and clinical application. *Sports Med Arthrosc* 2008; 16(4):217-20.

Specialty Matched Consultant Advisory Panel review 7/2010

Harris JD, Cavo M, Brophy R et al. Biological Knee Reconstruction: A Systematic Review of Combined Meniscal Allograft Transplantation and Cartilage Repair or Restoration. Arthroscopy 2011; 27(3):409-18.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 06/09/11

Specialty Matched Consultant Advisory Panel review 7/2011

American Academy of Orthopaedic Surgeons. Clinical practice guideline on the diagnosis and treatment of osteochondritis dissecans. 2010. Reviewed June 28, 2012 from http://www.aaos.org/research/guidelines/OCD_guideline.pdf

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 6/14/12

Specialty Matched Consultant Advisory Panel review 7/2012

Kon E, Filardo G, Di Matteo B et al. Matrix assisted autologous chondrocyte transplantation for cartilage treatment: A systematic review. Bone Joint Res 2013; 2(2):18-25. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3626217/

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 6/13/13

Specialty Matched Consultant Advisory Panel review 7/2013

Dunkin BS, Lattermann C. New and Emerging Techniques in Cartilage Repair: MACI. Oper Tech Sports Med. 2013 Jun 1;21(2):100-107. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3780415/

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 6/12/14

Specialty Matched Consultant Advisory Panel review 7/2014

Medical Director review 7/2014

Specialty Matched Consultant Advisory Panel review 6/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 6/11/15

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 10/15/15

Specialty Matched Consultant Advisory Panel review 6/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 4/13/17

Specialty Matched Consultant Advisory Panel review 6/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 12/14/17

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 4/12/18

Specialty Matched Consultant Advisory Panel review 6/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 4/8/2019

Specialty Matched Consultant Advisory Panel review 7/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 4/16/2020

Specialty Matched Consultant Advisory Panel review 6/2020

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.48, 4/8/2021

Specialty Matched Consultant Advisory Panel review 6/2021

Specialty Matched Consultant Advisory Panel review 6/2022

Makris EA, Gomoll AH, Malizos KN, et al. Repair and tissue engineering techniques for articularcartilage. Nat Rev Rheumatol. Jan 2015; 11(1): 21-34. PMID 25247412

Simon TM, Jackson DW. Articular Cartilage: Injury Pathways and Treatment Options. Sports MedArthrosc Rev. Mar 2018; 26(1): 31-39. PMID 29300225

US FDA Approved Cellular and Gene Therapy Products. MACI (Autologous Cultured Chondrocytes on aPorcine Collagen Membrane).

US FDA Device Approvals, Denials and Clearances. Agili-C - P210034. Updated April 29, 2022.

Specialty Matched Consultant Advisory Panel 6/2023

Medical Director Review 6/2023

Policy Implementation/Update Information

For Policy Titled: Autologous Chondrocyte Transplantation

4/96 Original Policy issued

11/96 Reaffirmed: National Association reviewed 7/96. Remains investigational.

6/98 Reaffirmed: National Association reviewed 2/98. Remains investigational.

5/99 Policy reviewed by MPAG and approved for specific indications.

7/99 Reformatted. Medical Term Definitions added.

10/00 Specialty Matched Consultant Advisory Panel. Added alternatives to description section of policy. System coding changes. Medical Policy Advisory Group review. No changes to criteria. Approve.

12/00 New 2001 HCPCS code J7330 added. System coding changes.

9/02 Specialty Matched Consultant Advisory Panel meeting 8/14/2002. Revised under the when it is not covered section to include any indications other than those listed above. Typos corrected. Format changes. Code S2109 deleted from the Billing/Coding Section. System coding changes.

12/03 Benefits Application and Billing/Coding sections updated for consistency.

1/04 Individual CPT codes listed for CPT code ranges 29870-29887 under Billing/Coding section.

7/29/04 HCPCS code S2112 added to Billing/Coding section.

8/12/04 Specialty Matched Consultant Advisory Panel review 07/15/2004 with no changes made to policy criteria. References added. HCPCS code S2113 added to Billing/Coding section.

1/6/05 Code 27412 added to Billing/Coding section of policy.

3/02/06 Policy reviewed by Medical Policy Advisory Group with no changes 09/08/05.

8/21/06 Policy number added to Key Words. CPT codes and references updated. Specialty Matched Consultant Advisory Panel review 7/24/06. No changes to criteria. (adn)

8/25/08 Added Item 7 to Policy Guidelines section: Patient has had inadequate response to prior arthroscopic or other surgical repair. Specialty Matched Consultant Advisory Panel review 7/17/08. No change to policy statement. (adn)

For Policy Renamed: Autologous Chondrocyte Implantation

3/30/09 Policy renamed. Description section extensively revised. Coverage criteria revised to read: "Autologous chondrocyte implantation may be considered medically necessary for the treatment of disabling full thickness articular cartilage defects of the knee 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: The patient is skeletally mature 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), Focal, full thickness (grade III or IV) uni-polar 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, Normal knee biomechanics, or alignment and stability achieved concurrently with autologous chrondrocyte implantation, Absence of meniscal pathology." Patellar and talar lesions added to list of noncovered indications in the When Not Covered section. Revised the rationale for coverage in the Policy Guidelines section. (adn)

6/08/10 Description section extensively revised. Added new criteria to "When Autologous Chondrocyte Implantation is not covered", which states, "Autologous chondrocyte implantation for all other joints, including patellar and talar, or any other indications is considered investigational. Matrix-induced autologous chondrocyte implantation is considered investigational. Treatment of focal articular cartilage lesions with autologous or allogeneic minced cartilage is considered investigational." Updated Policy Guidelines. References updated. Removed Medical Policy number. (mco)

8/17/10 Specialty Matched Consultant Advisory Panel review 7/2010. (mco)

8/16/11 Specialty Matched Consultant Advisory Panel review 7/2011. Removed the following coverage criteria from "When Covered" section: "Absence of meniscal pathology." Added the following statement to Policy Guidelines: "In addition, meniscal allograft transplantation may be performed in combination, either concurrently or sequentially, with autologous chondrocyte implantation." References updated. (mco)

8/7/12 Specialty Matched Consultant Advisory Panel review 7/2012. References updated. No changes to Policy Statements. (mco)

8/13/13 References to "minced cartilage" and "allogenic chondrocytes" deleted from this policy and can now be referenced in the BCBSNC policy titled, "Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions." Description section updated. The following statement removed from the "When not Covered" section: "Treatment of focal articular cartilage lesions with autologous or allogeneic minced cartilage is considered investigational." Policy Guidelines updated. References updated. Specialty Matched Consultant Advisory Panel review 7/2013. Medical Director review 7/2013. (mco)

8/12/14 Specialty Matched Consultant Advisory Panel review 7/2014. Medical Director review 7/2014. References updated. Description section and Policy Guidelines updated. No changes to Policy Statements. (mco)

7/28/15 Reference added. Related policies added. Specialty Matched Consultant Advisory Panel review 6/24/2015. (sk)

12/30/15 Reference added. Autologous chondrocyte implantation of the patella considered medically necessary; need for a prior surgical procedure removed from the policy statement. (sk)

7/26/16 Specialty Matched Consultant Advisory Panel review 6/29/2016. (sk)

5/26/17 Reference added. Rationale extensively revised to focus on available products. Investigational statement on matrix-induced autologous chondrocyte implantation removed. (sk)

7/28/17 Specialty Matched Consultant Advisory Panel review 6/28/2017. (sk)

1/26/18 Reference added. (sk)

7/13/18 Reference added. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 6/27/2018. (sk)

8/27/19 Reference added. Specialty Matched Consultant Advisory Panel review 7/30/2019. (sk)

8/11/20 Reference added. Specialty Matched Consultant Advisory Panel review 6/17/2020. (sk)

7/1/21 Description section updated. Related Policy removed. Specialty Matched Consultant Advisory Panel review 6/16/2021. (sk)

7/26/22 Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 6/29/2022. (sk)

6/30/23 Reference added. Description section updated with minor edits. Minor edits to Policy Guidelines. Specialty Matched Consultant Advisory Panel review 6/2023. Medical Director review 6/2023. (rp)