

## Corporate Medical Policy

### Autologous Chondrocyte Implantation

<b>File Name:</b>	autologous_chondrocyte_implantation
<b>Origination:</b>	4/1996
<b>Last CAP Review:</b>	7/2011
<b>Next CAP Review:</b>	7/2012
<b>Last Review:</b>	7/2011

### Description of Procedure or Service

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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 or allogeneic chondrocytes, minced cartilage, 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, "Osteochondral Grafting in the Treatment of 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 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. A periosteal flap is removed from the proximal medial tibia and sutured to the surrounding rim of normal cartilage. The cultured chondrocytes are then injected beneath the periosteal flap.

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. At the present time, only Carticel (Genzyme) 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

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labeling suggests a more restricted use of autologous chondrocyte, i.e., 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 debridement, 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. These include Chondroselect (characterized chondrocyte implantation, TiGenex, Phase III trial), BioCart II (ProChon Biotech, Phase II trial), Cartilix (polymer hydrogel, Cartilix), MACI® (matrix-induced ACI, Verigen, available outside of the United States), Cartipatch (solid scaffold with an agarose-alginate matrix, TBF Tissue Engineering, Phase III trial), NeoCart (ACI with a 3-dimensional chondromatrix, Histogenics, Phase II trial), Hyalograft C (ACI with a hyaluronic acid-based scaffold, Fidia Advanced Polymers), and CAIS (Cartilage Autograft Implantation System, which harvests cartilage and disperses chondrocytes on a scaffold in a single stage treatment, Johnson and Johnson). Although clinical use of these second-generation ACI products has been reported in Europe, none are approved for use in the United States at this time.

DeNovo NT Graft (Natural Tissue Graft) and DeNovo® ET Live Chondral Engineered Tissue Graft (Neocartilage) are produced by ISTO Technologies with exclusive distribution rights by Zimmer. DeNovo NT consists of manually minced cartilage tissue pieces obtained from juvenile allograft donor joints. The tissue fragments are mixed intra-operatively with fibrin glue before implantation in the prepared lesion. It is thought that mincing the tissue helps with cell migration from the extracellular matrix and with fixation. As there is no use of chemicals and minimal manipulation, the allograft tissue does not require FDA approval for marketing. DeNovo NT is currently available in the U.S. and 4 U.S. sites are participating in a company-sponsored observational study with 25 subjects; the expected completion is 2013. DeNovo® ET graft (Neocartilage) uses juvenile allogeneic cartilage cells engineered by ISTO Technologies. The FDA approved ISTO's Investigational New Drug (IND) application for Neocartilage in 2006, which allowed them to pursue clinical trials of the product in humans.

**\*\*\*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

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**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

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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.

### When Autologous Chondrocyte Implantation is covered

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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

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following criteria are met:

1. 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),
2. 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 cm<sup>2</sup> 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

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

- Patellar and 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.

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.

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## Policy Guidelines

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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<sup>2</sup>; many studies treated lesions as large as 15cm<sup>2</sup>. Severe obesity (body mass index > 35 kg/m<sup>2</sup>), 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.

Although long-term studies are lacking, evidence indicates that ACI can improve symptoms in some patients with lesions of the articular cartilage of the knee who have failed prior surgical treatment. These patients, who are too young for total knee replacement, have limited options. Therefore, based on the clinical input, highly suggestive evidence from randomized controlled trials and prospective observational studies, combined with contextual factors, it is concluded that ACI may be considered an option for disabling full thickness chondral lesions of the knee caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior marrow stimulation procedure. Evidence is currently insufficient to evaluate the efficacy of ACI in comparison with other surgical repair procedures as a primary treatment of large lesions, or to evaluate the efficacy of ACI for joints other than the knee.

Results from second generation ACI procedures (MACI) from Europe appear promising. These products use a variety of biodegradable scaffolds and have the potential to improve consistent hyaline cartilage formation and reduce complications associated with injection under a periosteal patch. To date no MACI products are approved in the United States; therefore, these are considered investigational. Minced cartilage techniques are in the early stages of development and testing and are not approved in the United States; these are considered investigational.

## Billing/Coding/Physician Documentation Information

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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](http://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

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**For Policy Titled: Autologous Chondrocyte Transplantation**

TEC Bulletin - 3/96

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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

Carticel™ (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. Retrieved on July 14, 2004 from [http://www.ta.ecri.org/Med\\_Tech/Prod/static/422146.pdf](http://www.ta.ecri.org/Med_Tech/Prod/static/422146.pdf).

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/page.aspx?0=TA089>.

ECRI Custom Hotline Response. (February 2006). Osteochondral Autograft Transplantation in the Knee. Retrieved April 3, 2006 from [http://www.ta.ecri.org/Hotline/Prod/summary/detail.aspx?e=6&doc\\_id=9116](http://www.ta.ecri.org/Hotline/Prod/summary/detail.aspx?e=6&doc_id=9116)

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

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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

## Policy Implementation/Update Information

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### 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.

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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 cm<sup>2</sup> 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 chondrocyte 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)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.