COVERAGE:

Autologous Chondrocyte Transplantation (ACT) may be medically necessary when ALL of the following criteria are met:

1. symptomatic, full thickness cartilaginous defects, not involving the bone, caused by acute or repetitive trauma that found on the load bearing surface of the distal femur (medial or lateral femoral condyle lesions or troclear lesions)
2. cartilage defect(s) involve the weight-bearing surfaces of the knee
3. clinically significant symptoms of cartilage injury (acute or chronic) have been present for greater than one (1) year, with the presence of disabling pain, swelling, and/or knee locking/catching that are unresponsive to physical therapy, conservative treatment, prior arthroscopic or other surgical (micro-fraction, drilling, abrasion) repair procedure(s)
4. defect measuring less than six (6) centimeters in length, less than seven (7) millimeters in depth, and area size ranging from lower limit of three (3) and upper limit of ten (10) centimeters squared
5. opposing surface lesions (known as kissing lesions) less than grade III on either the tibial surface for the femoral condyle lesion and/or patellar surface for the trochlear lesion
6. between the ages of 15 to 45 years old
7. body mass index of less than 30
8. confirmation of at least 1/3 (one third) intact posterior meniscal rim
9. operative site is infection-free
10. no evidence of cartilage defects in areas, other than the knee, such as the ankle
11. no evidence of osteoarthritis or inflammatory disease(s), including rheumatoid arthritis
12. no history of malignancy in bones, cartilage, fat, or muscle in the treated leg
13. no evidence of lesions located on any non-weight bearing areas throughout the body
14. no evidence of sensitivities or allergies to gentamicin or bovine originated materials
15. knee must be stable and aligned with normal joint spacing, or undergoing simultaneous stabilization and alignment.

Documentation Required for Review:

1. progress, History, and/or Operative Notes confirming injury and prior treatments/therapies
2. report(s) of standing x-rays documenting normal alignment of the knee and the absence of osteoarthritis
3. photographs from knee arthroscopy showing the presence of the cartilage defect and normal cartilage surrounding the defect.

ACT is considered experimental, investigational or unproven for all other indications, including but not limited to:
1. other lesions of the knee (patellar or talar)
2. osteochondritis dissecans which involves both cartilage and bone
3. degenerative joint disease (osteoarthritis) or inflammatory disease(s) (rheumatoid arthritis
4. lesions of other body joints (such as the ankle).

**COVERAGE FOR REPEATED PROCEDURES:**

Coverage for a second or additional ACT procedure will not be allowed when there is evidence of persistence of continued, avoidable, repetitive trauma. This procedure limitation is in place whether or not the previous procedure was covered under the current benefit plan.

**NOTE ON PATIENT SELECTION CRITERIA:**

Currently, there is not general agreement on patient selection criteria for ACT. The selection criteria in this policy are based on available evidence about the efficacy and durability of ACT, to allow consistent coverage determinations of individual cases. Three FDA-required studies in-progress (a registry-based study, the Study of the Treatment of Articular Repair and the Periosteal Study), but none have not yet concluded, or been peer-reviewed, or published in the scientific literature.

**DESCRIPTION:**

**Autologous Chondrocyte Transplantation (ACT),** also known as Autologous Chondrocyte Infusion/Implantation (ACI), is a surgical treatment for deep cartilage defects of the knee caused by acute or repetitive trauma. The intent of the transplantation is to replace defective articular cartilage with cultured chondrocyte cells that will produce new articular cartilage, displaying similar composition and properties to the original tissue. The ACT process involves three distinct and major stages (obtaining chondrocytes, culturing chondrocytes, and transplanting chondrocytes). The steps involved in the procedure process are:

1. Arthroscopy (first operative session) is performed to evaluate the suspected knee lesion or injury.
2. A region of healthy articular cartilage is identified during the Arthroscopy.
3. A biopsy of healthy cartilage (approximately 300 to 500 milligrams) is taken from the upper-medial or upper-lateral femoral condyle of the damaged knee.
4. The healthy cartilage is minced and chemically (enzymatically) digested.
5. The chondrocytes are separated and isolated.
6. The chondrocytes are allowed to cultivate in a culture medium for 11 to 21 days until 12 million cells are isolated, after which the cultured chondrocytes are suspended in liquid for injection.
7. During a medial or lateral parapatellar arthrotomy (second operative session) under general...
8. The patient is kept non-weight bearing for a period of 4 to 6 weeks followed by a 2 to 3 week period of partial weight bearing and finally an intense physical therapy regimen for the remainder of a one year post operative period.

FOOD AND DRUG ADMINISTRATION (FDA) CLARIFICATION:

The culturing of chondrocytes is considered by the FDA to fall into the category of manipulated autologous structural (MAS) cells, which are subject to a biologic licensing requirement.

The FDA has developed a policy on the review of safety and effectiveness of MAS cells. At the present time, only Carticel™ has received FDA accelerated approval for the culturing of chondrocytes through a biologic license. The approval indications and usage as cited in the Carticel package insert are as follows:

1. "Carticel has been approved for the repair of clinically significant, symptomatic cartilaginous defects of the femoral condyle (medial, lateral or trochlear) caused by acute or repetitive trauma;"
2. "Carticel is not indicated for the treatment of cartilage damage associated with osteoarthritis;" and
3. "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."

In 1999, the Genzyme Tissue Repair (GTR) was convinced their ability to conduct randomized, controlled trials could not be completed due to the substantial difficulty enrolling patients in these types of studies. GTR opted to discontinue their efforts to redesign and perform studies they were certain were impossible to perform. They have proposed to the FDA that the labeling indication for Carticel be narrowed to patients who have had an inadequate response to prior arthroscopic or other surgical repair procedures. This proposal is known to be "ACT as Second-Line Therapy".

On November 4, 1999, the FDA announced a labeling change for Carticel rescinding their earlier requirement for randomized controlled studies, but still requiring that outcomes studies be done on patients having ACT with comparison to their previous treatments.
ADDITIONAL INFORMATION ON DIAGNOSIS AND CONVENTIONAL TREATMENT: 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 (degenerative arthritis) 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, micro-fracture and abrasion arthroplasty.

RATIONALE:

Previous literature assessments conclude that there was insufficient evidence to permit conclusions concerning the health outcomes associated with ACT for the following reasons:

1. The available studies do not consistently report all the information needed to assess the results and efficacy of ACT;
2. The available data are based on two single-arm series with incomplete follow-up and no concurrent control groups; and
3. The lack of controls for prior surgical management, adjunctive procedures, intensity of rehabilitation, and prognosis for improvement further confound the determination of treatment effect.

The FDA reported approval of Carticel primarily on case reports of 153 patients treated in Sweden. Of patients who were followed for at least 18 months after the treatment, about 70% showed improvement. Biopsies were done on 22 patients with Carticel. Fifteen showed hyaline cartilage development post therapy. Over one half of the patients who had failed to benefit from earlier surgical intervention without Carticel, had longer lasting improved outcomes when Carticel was included in the procedure.

While ACT appears to be a promising alternative to the standard approaches for cartilage defects of the knee, the efficacy and long-term outcomes remain unknown. Well-designed, randomized, controlled trials are required to prove the efficacy, continue to define patient selection criteria, and document the long-term outcomes when compared to alternative therapies. At the present time, ACT is a treatment plan ONLY for carefully selected patients. This is a listing of the Patient Selection Criteria with the corresponding Rationale:

1. Between the ages of 15 to 45 years old at the time of surgery. RATIONALE: Bone maturity is incomplete for patients younger than 15 years of age – implanting cartilage cells may affect bone growth and the results of the procedure. With age, the quality of the cartilage in the knee worsens – implanting poor-quality cartilage cells may affect results of the procedure.
2. Body mass index of < 30. RATIONALE: Increased body weight increases strain and stress of the knee resulting in inadequate rehabilitation following the procedure and decreasing the...
durability of the procedure.

3. Clinically significant symptoms of cartilage for > one year, with the presence of disabling pain, swelling, and/or knee locking/catching that are unresponsive to physical therapy, conservative treatment, prior arthroscopic or surgical (micro-fraction, drilling, abrasion) repair procedures. **RATIONALE:** Usual symptoms such as pain or “locking” of the joint may improve over time without surgery and with conservative treatment.

4. Knee must be stable and aligned with normal joint spacing. **RATIONALE:** If the knee is not stable (ligaments and other structures) it is not possible to determine whether the symptoms are related to the knee’s instability or to cartilage defects. Unstable knees may affect the results of the procedure.

5. The cartilage defect must be < 6 centimeters in length, < 7 millimeters in depth, and total area size ranged from lower limit of 3 to upper limit of 10 centimeters squared. **RATIONALE:** Small cartilage defects are not likely to cause significant problems and symptoms may improve without surgical intervention.

6. Full thickness cartilaginous, not the bone, defects found on the load bearing surface of the distal femur (medial or lateral femoral condyle lesions or trochlear lesions). **RATIONALE:** If more than cartilage is involved, adding back more cartilage may not solve the problem. The bone underneath the problem cartilage must be adequate since cartilage cannot directly replace missing bone.

7. The cartilage defect(s) involve the weight-bearing surface of the knee called the femoral condyles. Other parts of the knee, including the area underneath the kneecap (patellofemoral joint) and the lower part of the knee joint (tibial articular cartilage) are normal. These areas including opposing surface lesions (known as kissing lesions) located on either side of the tibial surface of the femoral condyle and/or patellar surface. **RATIONALE:** There is less scientific data regarding other joints in the knee to determine whether health outcomes would be improved with ACT. The FDA has only approved the Carticel product for use on the femoral condyle (medial, lateral or trochlear aspects). If other parts of the knee abnormal, the results of ACT on the femoral condyle may be affected.

8. Operative site is infection-free. **RATIONALE:** Cultured chondrocytes introduced into a compromised infectious operative site can affect the integrity of new articular cartilage.

9. Osteochondritis dissecans which involves both cartilage and bone is not suitable for ACT and is not covered. **RATIONALE:** If the osteochondritis dissecans has happened in the past and the bone is now normal, this exclusion does not apply.

10. Degenerative joint disease (osteoarthritis) or inflammatory disease(s) (rheumatoid arthritis) is not suitable for ACT and is not covered. **RATIONALE:** These types of conditions may not respond to this procedure and the FDA has not approved the Carticel product for these indications.

11. No evidence of cartilage defects in areas, other than the knee, such as the ankle. **RATIONALE:** The FDA has only approved the Carticel product for used on the femoral
condyle (medial, lateral or trochlear aspects).

12. No history of malignancy in bones, cartilage, fat, or muscle in the treated leg.  
   **RATIONALE:** Prior malignancies of the treated leg may not facilitate new articular cartilage development and the FDA has not approved the Carticel product when given following a malignancy diagnosis.

13. No history of sensitivities or allergies to gentamicin or anaphylactic response to bovine originated materials.  **RATIONALE:** The FDA approved labeled approval warns that the Carticel product should not be given to patients with a known history of anaphylaxis to gentamicin or known sensitivities to materials of bovine origin.

14. The patient must be capable of following the rigorous post-procedure rehabilitation protocol and should cease participation in those activities that resulted in the cartilage damage.  
   **RATIONALE:** The outcome of the procedure may be affected by inadequate rehabilitation following the procedure and the durability of the procedure may be adversely affected by continued, avoidable, repetitive trauma. Coverage for a second or additional ACT procedure will not be allowed when there is evidence of persistence of continued, avoidable, repetitive trauma. This procedure limitation is in place whether or not the previous procedure was covered under the current benefit plan.

15. Documentation is required for review of medical necessity, which includes patient chart notes confirming injury and prior treatments and therapies, x-ray reports documenting normal alignment and absence of osteoarthritis, and photographs showing the presence of the cartilage defect and normal cartilage surrounding the knee.  **RATIONALE:** Documentation confirms prior conservative and/or surgical treatments/therapies and current knee anatomy. Normal cartilage surrounding the defect is critical to carry the increasing weight bearing load during rehabilitation. The cartilage defect must be clearly visible and distinctly measurable. The photodocumentation should occur at the time of the arthroscopy to harvest chondrocytes.

**NOTE:** Additional procedures may be done during the second operative session; arthrotomy, such as repair of ligaments or tendons, or recreation of osteotomy for realignment of the joint. Therefore it may be difficult to attribute the outcomes entirely to the chondrocyte transplant procedure.

Inasmuch, as there are currently no generally agreed upon patient selection criteria, these patient selection criteria are based on the best available evidence on the efficacy and durability of ACT. They were developed to allow rational coverage determinations for individual cases, even though the published evidence of efficacy and durability is incomplete. Three FDA-required studies in-progress (a registry-based study, the Study of the Treatment of Articular Repair and the periosteal study) have not yet concluded, nor been peer-reviewed, nor published in the scientific literature.

**PRICING:**

*Blue Cross and Blue Shield of Texas, a Division of Health Care Service Corporation, a Mutual Legal Reserve Company*
*Southwest Texas HMO, Inc.* *d/b/a HMO Blue* Texas
*Independent Licensees of the Blue Cross and Blue Shield Association*
There is NO specific diagnosis code to describe the specific diagnosis criteria listed in the coverage section. The diagnosis code would need to document the current step of the multi-phased procedure.

The charges for the culturing component of the procedure may be submitted as part of the hospital claim.

REFERENCES:

Autologous Chondrocyte Transplantation of the Knee. BCBSA TEC Assessment Program (2003 June) 18(2): 1-79.

DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.
HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.