Policy Statement

Meniscal allograft transplantation may be considered medically necessary in patients who have had a prior meniscectomy and have symptoms related to the affected side, when all of the following criteria are met:

- 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)
- Disabling knee pain with activity that is refractory to conservative treatment
- Absence or near absence (greater than 50%) of the meniscus, established by imaging or prior surgery
- Documented minimal to absent diffuse degenerative changes in the surrounding articular cartilage (e.g., Outerbridge grade II or less, less than 50% joint space narrowing)
- Normal knee biomechanics, or alignment and stability achieved concurrently with meniscal transplantation

Meniscal allograft transplantation may be considered medically necessary when performed in combination, either concurrently or sequentially, with treatment of focal articular cartilage lesions using any of the following procedures:

- Autologous chondrocyte implantation
- Osteochondral allografting
- Osteochondral autografting

Use of other meniscal implants incorporating materials such as collagen and polyurethane are considered investigational.

Policy Guidelines

Patients should exhibit symptoms of persistent disabling knee pain that has not adequately responded to physical therapy and analgesic medications. Uncorrected 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.

Severe obesity (e.g., body mass index greater than 35 kg/m²) may affect outcomes due to the increased stress on weight-bearing surfaces of the joint. Meniscal allograft transplantation is typically recommended for young active patients who are too young for total knee arthroplasty.

Coding

There is a CPT category I code specific to this procedure when performed arthroscopically:

- 29868: Arthroscopy, knee, surgical; meniscal transplantation (includes arthrotomy for meniscal insertion), medial or lateral

There is no CPT code for implantation of the ReGen Collagen Scaffold, but the American Academy of Orthopaedic Surgeons' Coding, Coverage and Reimbursement Committee has recommended that CPT code 29868 for meniscal transplantation is appropriate for this procedure.

Description

Meniscal allografts and other meniscal implants (e.g., collagen) are intended to improve symptoms and reduce joint degeneration in patients who have had a total or partial meniscus resection.
Related Policies

- Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions
- Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Collagen Meniscus Implants

In 2008, the ReGen Collagen Scaffold was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA determined that this device was substantially equivalent to existing absorbable surgical mesh devices. The ReGen Collagen Scaffold (also known as MenaFlex™ CMI) was the only collagen meniscus implant (CMI) with the FDA clearance at that time. Amid controversy about this 510(k) clearance decision, the FDA reviewed its decision. In October 2010, the FDA rescinded the approval, stating that MenaFlex™ is intended for different purposes and is technologically dissimilar from the predicate devices identified in the approval process. The manufacturer appealed the rescission, and won its appeal in 2014. The product, now called CMI®, is manufactured by Ivy Sports Medicine. CMI® is the only FDA-approved collagen meniscus product currently on the market. FDA product code: OLC.

Rationale

Background

Meniscal Cartilage Damage

Meniscal cartilage is an integral structural component of the human knee, functioning to absorb shocks and providing load sharing, joint stability, congruity, proprioception, and lubrication and nutrition of the cartilage surfaces. Total and partial meniscectomy frequently result in degenerative osteoarthritis. The integrity of the menisci is particularly important in knees in which the anterior cruciate ligament has been damaged. In these situations, the menisci act as secondary stabilizers of anteroposterior and varus-valgus translation.

Treatment

Meniscal allograft transplantation (MAT) is considered a salvage procedure, reserved for patients with disabling knee pain following meniscectomy who are considered too young to undergo total knee arthroplasty or in patients who require a total or near total meniscectomy for irreparable tears. As a result, the population intended to receive these transplants is relatively limited. Using a large database of privately insured non-Medicare patients, Cvetanovich et al (2015) estimated an annual incidence of MAT in the United States of 0.24 per 100,000.¹ It is not expected that clinical trials will be conducted to compare meniscal allografts with other orthopedic procedures, although trials comparing allograft transplant with medical therapy are possible.
There are 3 general groups of patients who have been treated with MAT:

- young patients with a history of meniscectomy who have symptoms of pain and discomfort associated with early osteoarthritis that is localized to the meniscus-deficient compartment
- patients undergoing anterior cruciate ligament reconstruction in whom a concomitant meniscal transplant is intended to provide increased stability
- young athletes with few symptoms in whom the allograft transplantation is intended to deter the development of osteoarthritis. Due to the risks associated with this surgical procedure, prophylactic treatment for this purpose is not frequently recommended

Issues under study include techniques for processing and storing the grafts, proper sizing of the grafts, and appropriate surgical techniques. The 4 primary ways of processing and storing allografts are fresh viable, fresh frozen, cryopreserved, and lyophilized. Fresh viable implants, harvested under sterile conditions, are less frequently used because the grafts must be used within a couple of days to maintain viability. Alternatively, the harvested meniscus can be fresh frozen for storage until needed. Cryopreservation freezes the graft in glycerol, which aids in preserving the cell membrane integrity and donor fibrochondrocyte viability. Cryolife is a commercial supplier of such grafts. Donor tissues may also be dehydrated (freeze-dried or lyophilized), permitting storage at room temperature. Lyophilized grafts are prone to reduced tensile strength, shrinkage, poor rehydration, post transplantation joint effusion, and synovitis; they are no longer used in the clinical setting. Several secondary sterilization techniques may be used, with gamma irradiation the most common. The dose of radiation considered effective has been shown to change the mechanical structure of the allograft; therefore, nonirradiated grafts from screened donors are most frequently used. In a survey conducted by the International Meniscus Reconstruction Experts Forum, when surgeons were asked about allograft preference, 68% preferred fresh frozen nonirradiated allografts, with 14% responding fresh viable allografts.2

There are several techniques for MAT; most are arthroscopically assisted or all-arthroscopic. Broadly, the techniques are either all-suture fixation or bone fixation. Within the bone fixation category, the surgeon may use either bone plugs or a bone bridge. Types of bone bridges include keyhole, trough, dove-tail, and bridge-in-slot. The technique used depends on laterality and the need for concomitant procedures. Patients with malalignment, focal chondral defects, and/or ligamentous insufficiency may need concomitant procedures (ostectomy, cartilage restoration, and/or ligament reconstruction, respectively).3

Tissue engineering that grows new replacement host tissue is also being investigated. For example, the Collagen Meniscus Implant (Ivy Sports Medicine, formerly the ReGen Collagen Scaffold by ReGen Biologics), is a resorbable collagen matrix composed primarily of type I collagen from bovine Achilles tendons. The implant is provided in a semilunar shape and trimmed to size for suturing to the remaining meniscal rim. The implant provides an absorbable collagen scaffold that is replaced by the patient’s soft tissue; it is not intended to replace normal body structure. Because it requires a meniscal rim for attachment, it is intended to fill meniscus defects after a partial meniscectomy. Other scaffold materials and cell-seeding techniques are being investigated. Nonabsorbable and nonporous synthetic implants for total meniscus replacement are in development. One total meniscus replacement that is in early phase clinical testing is NUSurface® (Active Implants); it is composed of a polyethylene reinforced polycarbonate urethane.

Outcome Measures
The outcomes of this treatment (i.e., pain, functional status) are subjective, patient-reported outcomes that are prone to placebo effects. On the other hand, the natural history of a severely damaged meniscus is predictable, with progressive joint damage, pain, and loss of function.

Literature Review
Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of
life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The primary literature consists of retrospective case series and systematic reviews of these case series. Two main issues are investigated: (1) Does meniscal allograft transplantation (MAT) reduce pain and improve function? and (2) Does this procedure reduce joint degeneration?

Meniscal Allograft Transplantation
Systematic Reviews
Several systematic reviews of available case series have reported reductions in pain and improvements in function at mid-term follow-up, with failure rates at the time of follow-up ranging from 7% to 35% (see Table 1). Elattar et al (2011) published a large systematic review with a total of 1136 allografts. Twelve different clinical scoring systems were described, which generally showed reductions in pain and improvements in function. Hergan et al (2011) conducted a systematic review of the literature to evaluate the characteristics of patients, graft survival, and clinical outcomes. The analysis found that patients with Outerbridge scores of II or less in any area had significantly improved post treatment Lysholm Knee Score (LKS) and Tegner Activity Scale (TAS) scores, whereas patients with Outerbridge grade III or more in any area (not repaired) did not. Studies that analyzed patients undergoing concomitant procedures did not detect a difference between subgroups compared with MAT alone. Functional outcomes were considered generally good where reported. Rosso et al (2015) published a systematic review evaluating 55 studies (total N=1623 patients). Data from 37 studies were included in demographic and outcome analyses. Collectively, these systematic reviews, which are based primarily on level IV evidence, summarize the short- to medium-term outcomes of MAT (see Table 1).

Table 1. Summary of Key Systematic Reviews of MAT

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>No. and study type</td>
<td>44 cohort and case series</td>
<td>14 cohort and case series with minimum 2-y follow-up</td>
<td>55 (2 level II, 7 level III, 46 level IV)</td>
</tr>
<tr>
<td>Population</td>
<td>1136 knees (1068 patients)</td>
<td>196 knees</td>
<td>1623 patients</td>
</tr>
<tr>
<td>Follow-up (range)</td>
<td>4.6 y (8 mo to 20 y)</td>
<td>53.8 mo (24-167 mo)</td>
<td>53.6 mo (12-168 mo)</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>Pain and function</td>
<td>Pain and function</td>
<td>Pain and function</td>
</tr>
<tr>
<td>Review synthesis</td>
<td>All showed clinical improvement</td>
<td>Alleviation of knee pain and improvement in function noted</td>
<td>Weighted pre-/postmeasures⁵: • VAS pain score decreased from 6.4 to 2.4 • LKS increased from 55.5 to 82.7</td>
</tr>
<tr>
<td>Pain and function</td>
<td>10.6%</td>
<td>7%-35%</td>
<td></td>
</tr>
<tr>
<td>Failure rate</td>
<td>Fresh frozen: 9.9%</td>
<td>Cryopreserved: 18.2%</td>
<td></td>
</tr>
</tbody>
</table>
### Randomized Controlled Trials

Smith et al (2018) reported on the results of a small RCT that randomized 21 patients with a symptomatic meniscal deficient knee to MAT (n=10) or personalized physical therapy (n=11). Another 15 patients who were screened for the RCT decided instead to choose their treatment (referred to as a preference group) received MAT (n=6) or personalized physical therapy (n=9). The Knee Injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee (IKDC) score, Lysholm Knee Scoring Scale score, and complications were collected at baseline, 4 and 8 months, and 1 year after the interventions. Trialists reported pooled results from the RCT and preference group, with statistically significant differences in favor of MAT group for KOOS composite score (mean difference, 12; p=0.03) and KOOS subscales of pain (mean difference, 15; p=0.02) and activities of daily living (mean difference, 18; p=0.005). However, pooling data from the RCT and preference group precluded a meaningful interpretation of data.

### Case Series

The characteristics and results of several case series with longer-term follow-up are provided in Tables 2 and 3. Verdonk et al (2005) published a large case series with long-term follow-up from 95% of their first 105 fresh cultured (viable) meniscal allografts. The indication for transplantation was moderate-to-severe pain in patients who had undergone previous total meniscectomy, not old enough to be considered for a knee joint replacement, and with good alignment of the lower limb and a stable joint (some were corrected concomitantly). In the study by Hommen et al (2007), concomitant procedures were performed in 75% of the patients, including anterior cruciate ligament reconstruction or revision (n=10), high tibial osteotomy (n=2), and lateral retinaculum release (n=3).

At a mean follow-up of 16 years, van der Wal et al (2009) reported graft survival decreased to 52.5%, while most failures in the study by Vundelinckx et al (2010) occurred approximately 10 years postoperatively. That said, at an average of 105 months of follow-up, the 34 remaining patients assessed in the Vundelinckx study showed significant reductions in pain and improvements in function relative to preoperative levels. Radiographic evidence reported by van der Wal also showed a slight or moderate increase in osteoarthritis in 42% of patients (1 or 2 points) and no increase in the other 58%. Of 15 patients with follow-up radiographs in the Hommen study, 10 (67%) had joint space narrowing, and 12 (80%) had progression of the Fairbank degenerative joint disease score in the transplanted tibiofemoral compartment.

### Table 2. Summary of Key Case Series Characteristics for MAT

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>105</td>
<td>57</td>
<td>34/49</td>
</tr>
</tbody>
</table>

---

a Data from 37 of the 55 studies in the systematic review.
**Section Summary: Meniscal Allograft Transplantation**

Evidence for the use of MAT in patients with disabling knee pain and a prior meniscectomy consists of systematic reviews of a large number of case series and an RCT. The reviews have found that MAT is associated with reductions in pain and improvements in function. Longer term studies have indicated that these improvements are maintained in a substantial percentage of patients, up to 10 years and beyond. Because the results of a single RCT, which enrolled a very small number of patients, pooled data from randomized and nonrandomized groups, results cannot be interpreted in a meaningful way. Adverse events, such as graft failure and the need for additional procedures, occur frequently. The strength of the evidence, including accurate estimates of the magnitude of benefit and the complication rates, are limited by the type of data available (case series and systematic reviews of these case series) as well as the heterogeneity in surgical techniques and patient characteristics across the studies.

**Mat Plus Articular Cartilage Repair**

Patients with malalignment, focal chondral defects, and/or ligamentous insufficiency may require additional surgery combined with MAT. When MAT is combined with osteotomy or articular cartilage repair in a single procedure, MAT should be performed first. The evidence available for the efficacy of MAT in knees with chondral damage consists of 1 prospective comparative study, case series, most of which are retrospective, and systematic reviews of case series.

**Systematic Reviews**

Harris et al (2011) published a systematic review of MAT plus cartilage repair or restoration (see Table 4). Patients underwent MAT with autologous chondrocyte implantation (ACI; n=73), osteochondral allograft (n=20), osteochondral autograft (n=17), or microfracture (n=3). All studies showed improvement in clinical outcomes at final follow-up compared with the preoperative condition. Outcomes were similar to historical outcomes, extracted from mid-term and long-term follow-up studies, of procedures performed in isolation. Additional surgeries are common (nearly 50%) after MAT plus cartilage repair or restoration procedures.

**Table 3. Summary of Key Case Series Outcomes for Meniscal Allograft Transplantation**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Mean age (range), y</td>
<td>35 (16-50)</td>
<td>39 (26-55)</td>
<td>33 (14-47)</td>
</tr>
<tr>
<td>Population</td>
<td>Previous total meniscectomy</td>
<td>Previous total meniscectomy</td>
<td>Patients with intact allograft</td>
</tr>
<tr>
<td>Intervention</td>
<td>MAT</td>
<td>MAT</td>
<td>MAT</td>
</tr>
<tr>
<td>Control</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Length of FU (range)</td>
<td>3-15 y</td>
<td>14 y (9-18 y)</td>
<td>105 mo</td>
</tr>
</tbody>
</table>

FU: follow-up; MAT: meniscal allograft transplantation.

**Table 4. Summary of Key Systematic Reviews**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Harris et al (2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. and study type</td>
<td>6 case series</td>
</tr>
<tr>
<td>Population</td>
<td>110</td>
</tr>
<tr>
<td>Intervention</td>
<td>MAT combined with cartilage repair or restoration</td>
</tr>
</tbody>
</table>
Variables | Harris et al (2011)\textsuperscript{12} |
---|---|
Control | Baseline to post treatment |
| Historical controls of procedures performed in isolation |
Outcome measures | Pain and function |
Review synthesis | Outcomes improved from baseline to posttreatment |
| 4/6 studies found outcomes equivalent to procedures performed in isolation |
| 2/6 studies found combined surgery not as good as historical controls |
Review conclusion | MAT can improve pain and function when combined with cartilage repair or restoration procedures |
Review limitations | Based on case series with historical controls |

MAT: meniscal allograft transplantation.

The largest and longest study to report on MAT in patients with significant (grade III and IV) chondral damage is that by Stone et al (2010) who reported mean allograft survival of 9.9 years (see Table 5).\textsuperscript{13} Other prospective studies have reported on graft survival and functional outcomes when MAT has been combined with articular cartilage repair.\textsuperscript{14,15}

**Case Series**

The following studies were published subsequent to the systematic review (see Table 5). Kempshall et al (2015) looked at MAT concomitant with cartilage repair procedures on (1) patients with more knee cartilage damage (grade 3b >1 cm\textsuperscript{2}) and (2) patients with less knee cartilage damage (grade 3b <1 cm\textsuperscript{2}).\textsuperscript{16} Functional outcomes following the procedures were similar between the 2 groups. However, implant survival (using graft failure as an end point) was lower among those with greater cartilage damage.

Ogura et al (2016) retrospectively reviewed patients who had undergone ACI and MAT.\textsuperscript{17} Seventeen patients were followed for a mean of 7.9 years. Significant improvements in clinical outcomes (visual analog scale for pain, Western Ontario and McMaster Universities Arthritis Index, 36-item Short-Form Health Survey, and modified Cincinnati Knee Rating Scale scores) were reported in 65% of the patients. Of the 6 procedures considered failures, 4 underwent TKA and 2 underwent revision surgery.

Zaffagnini et al (2016) reviewed 147 patients undergoing arthroscopic bone plug-free MAT, with 48% of patients having concomitant procedures (mostly high tibial osteotomy and anterior cruciate ligament reconstruction).\textsuperscript{18} Two survival analyses were conducted, one with the end point of surgical failure (need for revision procedures related to initial MAT) and the other with the end point of clinical failure (same revision procedures as a surgical failure or LKS less than 65 at final follow-up). Mean overall survival time with the surgical failure end point was 9.7 years (95% confidence interval, 9.1 to 10.3 years) and mean overall survival with the clinical failure end point was 8.0 years (95% confidence interval, 7.1 to 8.8 years). Logistic regression analysis did not reveal any variables (including concomitant procedures) affecting the surgical or clinical failure end points.

**Table 5. Series of MAT with Articular Cartilage Repair**

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>115</td>
<td>99</td>
<td>17</td>
<td>147</td>
</tr>
<tr>
<td>Population</td>
<td>Consecutive patients with grade III-IV chondral damage</td>
<td>Prospective series</td>
<td>Retrospective series</td>
<td>Retrospective series</td>
</tr>
<tr>
<td></td>
<td>• Grade 3b &lt;1 cm\textsuperscript{2}</td>
<td>• Grade 3b &gt;1 cm\textsuperscript{2}</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention</td>
<td>MAT</td>
<td>MACI and microfracture more common if chondral damage was 3c &gt;1 cm\textsuperscript{2}</td>
<td>ACI with MAT</td>
</tr>
<tr>
<td>Control</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
--- | --- | --- | --- | ---
Outcome measures | MAT survival | MAT survival | MAT survival | MAT survival
Length of FU | 5.8 y | 2 y | 5-10 y | 4 y
Results | Mean MAT survival, 9.9 y | Similar outcomes on KOOS, TAS, LKS, IKDC scores | Mean MAT survival rate, 75% at 5- and 10-y follow-up | Mean MAT survival range, 8-9.7 y
| 47% required additional surgery | MAT survival 97.9% if 3b <1 cm² and 78% if 3c >1 cm² | 67% (12/18) required additional surgery | 17% required additional surgery

**ACI:** autologous chondrocyte implantation; **FU:** follow-up; **IKDC:** International Knee Documentation Committee; **KOOS:** Knee Injury and Osteoarthritis Outcome Score; **LKS:** Lysholm Knee Score; **MACI:** matrix-assisted autologous chondrocyte implantation; **MAT:** meniscal allograft transplantation; **MCKRS:** modified Cincinnati Knee Rating Scale; **OAT:** osteochondral autograft transplantation; **SF-36:** 36-Item Short-Form Health Survey; **TAS:** Tegner Activity Scale; **VAS:** visual analog scale; **WOMAC:** Western Ontario and McMaster Universities Arthritis Index.

**Section Summary: MAT Plus Articular Cartilage Repair**

There is a limited amount of low-quality evidence on combined MAT and articular cartilage repair. The available literature has reported reductions in pain and improvements in functioning following these procedures, though studies have reported graft failures and the need for additional surgeries.

**Collagen Meniscus Implants**

A collagen meniscus implant (CMI) is sutured into place on a meniscal rim and is intended for use with a partial meniscectomy. Therefore, the literature search focused on controlled trials comparing health outcomes for CMI with partial meniscectomy alone. The literature to date consists of case series, a large RCT sponsored by a CMI manufacturer, a smaller RCT from Germany, and a small prospective comparative cohort study.

**Systematic Reviews**

Two systematic reviews, one by Harston et al (2012) and the other by Warth et al (2015), are summarized in Table 6. A third, by Zaffagnini et al (2015), focused only on studies assessing postoperative magnetic resonance imaging evaluations, which included 6 studies, none of which was an RCT and all of which were included in the Warth review. We do not discuss the Zaffagnini review further. Houck et al (2018) published the results of a systematic review that included multiple scaffold implantations including CMI. No studies in addition to those previously summarized by Warth were cited in this systematic review and Houck is not discussed further.

**Table 6. Summary of Key Systematic Reviews for CMI**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Search date</td>
<td>May 2011</td>
<td>March 2014</td>
</tr>
<tr>
<td>No. of studies</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Population</td>
<td>520</td>
<td>674</td>
</tr>
<tr>
<td>Intervention</td>
<td>321 patients received a CMI</td>
<td>439 patients received CMI</td>
</tr>
<tr>
<td>Control</td>
<td>Partial meniscectomy alone</td>
<td>32.3% patients had concomitant procedures</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>LKS, TAS, pain scales</td>
<td>LKS, TAS, pain scales</td>
</tr>
<tr>
<td>Length of FU</td>
<td>6-135 mo</td>
<td>3-152 mo</td>
</tr>
<tr>
<td>Review synthesis</td>
<td>66%-70% patients receiving CMI had satisfactory outcomes</td>
<td>CMI showed superior clinical outcomes vs partial meniscectomy alone</td>
</tr>
</tbody>
</table>
Variables | Harston et al (2012)\textsuperscript{19} | Warth et al (2015)\textsuperscript{20}
---|---|---
Outcomes in studies with control or comparison groups reported improvements in both groups | Several studies reported that meniscus scaffold decreased in volume over time | Reduced CMI size at last follow-up reported in 6 (54.5\%) of 11 studies | Second-look arthroscopy showed presence of newly formed meniscus-like tissue in area of the scaffold

Review limitations | Based on low-quality evidence | Mostly level IV evidence | No meta-analysis due to differing methodologies and data reporting across studies

CMI: collagen meniscus implant; FU: follow-up; LSK: Lysholm Knee Score; TAS: Tegner Activity Scale.

The quality of the studies included in the systematic reviews was generally rated as low. Tables 7 and 8 summarize select studies (2 RCTs, 2 cohort) included in the systematic reviews. A large RCT from the manufacturers of MenaFlex (Rodkey et al [2008]\textsuperscript{23}) was conducted under a Food and Drug Administration investigational device exemption. Only TAS scores in the chronic arm (but not the acute arm) differed significantly between the CMI and partial meniscectomy only groups. Kaplan-Meier analysis suggested a modest 10\% increase in survival in the chronic CMI group.

**Randomized Controlled Trials**

An independent research group published results from an RCT, reported by Linke et al (2006), comparing high tibial valgus osteotomy alone with osteotomy plus CMI.\textsuperscript{24} Arthroscopy in the CMI group showed 35\% complete healing, 30\% partial healing requiring resection of the posterior part of the implant, and 35\% with only small remains of the CMI left. Complications included implantation in insufficiently vascularized tissue, sutures cutting into the implant, inadequate fixation to the rim, destruction of the implant in an unstable knee joint or with premature loading postoperatively, allergic reaction to the xenogenic collagen implant, avulsion of the implant with joint blocking, and infection. Pain and function scores did not differ significantly between the CMI and control groups.

**Observational Studies**

Zaffagnini et al (2011) compared outcomes of 18 patients who chose CMI with 18 patients who chose partial medial meniscectomy, with a minimum 10-year follow-up.\textsuperscript{25} The 2 groups were comparable at baseline. No significant differences were found in the LKS and Yulish scores. Independent and blinded radiographic evaluation showed significantly less medial joint space narrowing in the CMI group (0.48 mm) than in the partial meniscectomy group (2.13 mm). This study had a potential for selection bias.

A retrospective review by Bulgheroni et al (2015) of 34 patients (17 CMI, 17 partial medial meniscectomies) found no significant differences between the groups for pain and function scores at an average of 9.6 years of follow-up.\textsuperscript{26}

**Table 7. Summary of Key Study Characteristics for CMI**

---|---|---|---|---|
Study design | RCT | RCT | Controlled cohort | Retrospective cohorts |
Sample size | 311 | 60 | 36 | 34 |
Population | Acute and chronic partial meniscectomy | Patient choice | Matched controls |
Intervention | CMI | Osteotomy plus CMI | CMI | CMI |
Control | Partial meniscectomy alone | Osteotomy alone | Partial meniscectomy alone | Partial meniscectomy alone |
Table 8. Summary of Key Study Results for CMI

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Length of FU (range)</td>
<td>59 mo (16-92 mo)</td>
<td>8-18 mo</td>
<td>133 mo (120-152 mo)</td>
<td>9.6 y</td>
</tr>
</tbody>
</table>

CMI: collagen meniscus implant; FU: follow-up; RCT: randomized controlled trial.

Section Summary: Collagen Meniscus Implants

Evidence for the use of CMI in patients undergoing partial meniscectomies consists of 2 systematic reviews, the most recent including 674 patients. The reviews reported overall positive results with CMI, but the quality of the included studies (RCTs and observational studies) was low. Radiologic evaluation showed destruction and/or absorption of the implant in a very large portion of patients.

Summary of Evidence

For individuals who are undergoing partial meniscectomy who receive meniscal allograft transplantation, the evidence includes systematic reviews of mostly case series and an RCT. Relevant outcomes are symptoms, functional outcomes, and quality of life. The systematic reviews concluded that most studies have shown statistically significant improvements in pain and function following the procedure. The benefits have also been shown to have a long-term effect (>10 years). Reviews have also reported acceptable complication and failure rates. There remains no evidence that meniscal allograft transplantation can delay or prevent the development of knee osteoarthritis. A limitation of the evidence is its reliance primarily on case series. Because the single RCT, which enrolled a very small number of patients, pooled data from randomized and nonrandomized groups, results cannot be interpreted in a meaningful way. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are undergoing partial meniscectomy and concomitant repair of malalignment, focal chondral defects, and/or ligamentous insufficiency who receive meniscal allograft transplantation, the evidence includes a systematic review of case series as well as case series published after the systematic review. Relevant outcomes are symptoms, functional outcomes, and quality of life. The systematic review concluded that pain and function improved following the procedure. One of the series published after the review showed that patients with more severe cartilage damage experienced favorable outcomes similar to patients with less cartilage damage. Another series published subsequently reported an overall 9.7-year survival of the implant. A limitation of the evidence is its reliance primarily on case series. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are undergoing partial meniscectomy who receive collagen meniscal implants, the evidence includes 2 systematic reviews primarily of case series. Relevant outcomes are symptoms, functional outcomes, and quality of life. The reviews reported overall positive results with the collagen meniscus implant, but the quality of the selected studies (RCTs,
observational studies) was low. Radiologic evaluations have shown reductions in the size of the implant in a large portion of patients. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Clinical Input 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.

**2011 Input**
In response to requests from Blue Cross Blue Shield Association, input was received from 1 physician specialty society (3 reviewers) and 3 academic medical centers 2011. Input considered combined meniscal allograft transplantation (MAT) and focal cartilage repair procedures to be medically necessary for patients younger than 55 years of age who have failed conservative treatment. Reviewers agreed that the collagen meniscus implant is investigational, although some considered it to be both investigational and medically necessary for some patients.

**2008 Input**
In response to requests from Blue Cross Blue Shield Association, input was received from 1 physician specialty society and 3 academic medical centers in 2008. Although long-term effects on joint space narrowing were unknown, all reviewers considered MAT to be beneficial in selected patients, with evidence of short to intermediate pain relief when performed in younger patients who had a prior meniscectomy and disabling knee pain. Contraindications noted were uncorrected instability, uncorrected malalignment, and the presence of significant articular disease.

**Practice Guidelines and Position Statements**

**International Meniscus Reconstruction Experts Forum**
In 2015, the International Meniscus Reconstruction Experts Forum published consensus statements on the practice of meniscal allograft transplantation (MAT) (see Table 9). The Forum’s statements included guidance on indications, graft procurement and preparation, surgical technique, and rehabilitation.

**Table 9. Select Consensus Statements on the Practice of MAT**

<table>
<thead>
<tr>
<th>Statements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications for MAT:</strong></td>
</tr>
<tr>
<td>• Unicompartmental pain post-meniscectomy</td>
</tr>
<tr>
<td>• In combination with anterior cruciate ligament reconstruction when meniscus deficient</td>
</tr>
<tr>
<td>• In combination with articular cartilage repair if meniscus deficient</td>
</tr>
<tr>
<td>Non-irradiated fresh frozen or fresh viable grafts are recommended.</td>
</tr>
<tr>
<td>Mechanical axis alignment should be performed prior to MAT; if mechanical axis deviation present, consider realignment osteotomy.</td>
</tr>
<tr>
<td>Based on current evidence, superiority of 1 surgical technique over another (all-suture vs bone) is not established.</td>
</tr>
</tbody>
</table>

**Outcome scores should include:**

- Disease-specific: Western Ontario Meniscal Evaluation Tool
- Region-specific: Knee injury and Osteoarthritis Outcome Score
- Activity: Marx Activity Rating Scale
- Quality of life/utility: EuroQoL 5 dimensions questionnaire

MAT: meniscal allograft transplantation; OA: osteoarthritis.
National Institute for Health and Care Excellence
The 2012 guidance from the National Institute for Health and Care Excellence stated that the evidence on “partial replacement of the meniscus of the knee using a biodegradable scaffold raises no major safety concerns,” but evidence for any advantage of the procedure over standard surgery was limited.27

American Academy of Orthopaedic Surgeons
The American Academy of Orthopaedic Surgeons updated its 2009 position in 2014, still recommending MAT for active people younger than 55 years old, with the goal of replacing the meniscus cushion before the articular cartilage is damaged.28 The website also notes that “synthetic (artificial) meniscal tissue has been tried, but there is conflicting information at this time.”

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

Medicare National Coverage
In 2010, the Centers for Medicare & Medicaid Services issued a national noncoverage determination for the collagen meniscus implant.29 A number of concerns regarding the efficacy and safety were raised by the Centers for Medicare & Medicaid Services analysis, which compared data reported to the Food and Drug Administration and published data. Concerns included an increased number of reoperations and a higher serious adverse event rate than in the control group. Centers for Medicare & Medicaid Services concluded that the collagen meniscus implant does not improve health outcomes in the Medicare population and that collagen meniscus implant is not reasonable and necessary for the treatment of meniscal injury or tear.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Currently, ongoing and unpublished trials that might influence this review are listed in Table 10.

Table 10. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>NCT01712191a Treatment of the Medial Meniscus with the Treatment of the Medial Meniscus with the NUSurface Meniscus Implant</td>
<td>150</td>
<td>Jun 2017 (ongoing)</td>
</tr>
<tr>
<td></td>
<td>NCT01059409 The Clinical and Medico-economical Evaluation of Meniscal Allografts in the Sequelae of Total or Sub-total Meniscectomy</td>
<td>120</td>
<td>Sep 2017 (ongoing)</td>
</tr>
<tr>
<td></td>
<td>NCT02136901a The VENUS Clinical Study (Verifying the Effectiveness of the NUSurface System): A Multi-center, Prospective, Randomized, Interventional Superiority Clinical Study</td>
<td>37</td>
<td>Feb 2019</td>
</tr>
</tbody>
</table>

NCT: National Clinical Trial.
*a Denotes industry-sponsored or cosponsored trial.

References


**Documentation for Clinical Review**

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Description of the knee structure (e.g., articular cartilage defects [including grade] and surrounding articular cartilage degenerative changes)
  - Knee biomechanics (i.e., stability and alignment) on physical exam
  - Reason patient is not a candidate for total knee arthroplasty
  - Prior treatment (surgical and non-surgical) and patient response(s)
  - Reason for requested procedure and planned treatment

- Progress notes specific to the condition and request (if applicable)

- Diagnostic radiology reports (including Outerbridge classification)

**Post Service**

- Operative report(s)

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

**MN/IE**

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.
### Type Code Description

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>29868</td>
<td>Arthroscopy, knee, surgical; meniscal transplantation (includes arthrotomy for meniscal insertion), medial or lateral</td>
</tr>
<tr>
<td>HCPCS</td>
<td>G0428</td>
<td>Collagen meniscus implant procedure for filling meniscal defects (e.g., CMI, collagen scaffold, Menaflex)</td>
</tr>
</tbody>
</table>

### ICD-10 Procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0SQC0ZZ</td>
<td>Repair Right Knee Joint, Open Approach</td>
</tr>
<tr>
<td>0SQC3ZZ</td>
<td>Repair Right Knee Joint, Percutaneous Approach</td>
</tr>
<tr>
<td>0SQC4ZZ</td>
<td>Repair Right Knee Joint, Percutaneous Endoscopic Approach</td>
</tr>
<tr>
<td>0SQD0ZZ</td>
<td>Repair Left Knee Joint, Open Approach</td>
</tr>
<tr>
<td>0SQD3ZZ</td>
<td>Repair Left Knee Joint, Percutaneous Approach</td>
</tr>
<tr>
<td>0SQD4ZZ</td>
<td>Repair Left Knee Joint, Percutaneous Endoscopic Approach</td>
</tr>
</tbody>
</table>

### Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/30/2015</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>05/01/2017</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>06/01/2017</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>06/01/2018</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
</tbody>
</table>

### Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

### Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national...
guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.