Medical Policy

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Title: Meniscal Allografts and Other Meniscus Implants

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Populations	Interventions	Comparators	Outcomes
Individuals: • Who are undergoing partial meniscectomy	Interventions of interest are: • Meniscal allograft transplantation	Comparators of interest are: • Partial meniscectomy without meniscal allograft transplantation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who are undergoing partial meniscectomy, and repair of malalignment, focal chondral defects, and/or ligamentous insufficiency	Interventions of interest are: • Meniscal allograft transplantation	Comparators of interest are: • Partial meniscectomy without meniscal allograft transplantation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who are undergoing partial meniscectomy	Interventions of interest are: • Collagen meniscal implants	Comparators of interest are: • Partial meniscectomy without meniscal implant	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life

DESCRIPTION

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

OBJECTIVE

The objective of this policy is to determine the net health outcome when meniscal allografts are used to treat patients with disabling knee pain following meniscectomy who are too young for total knee arthroplasty.

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 (OA). The integrity of the menisci is particularly important in knees in which the anterior cruciate ligament (ACL) 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 meniscal allograft transplantation:

- young patients with a history of meniscectomy who have symptoms of pain and discomfort associated with early osteoarthrosis that is localized to the meniscus-deficient compartment
- patients undergoing ACL 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 the most appropriate surgical techniques. Four 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 since 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 (Marietta, GA) is a commercial supplier of such grafts. Donor tissue 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 and 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, non-irradiated 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.[1]

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 (osteotomy, cartilage restoration, and/or ligament reconstruction, respectively).[2]

Tissue engineering that grows new replacement host tissue for individual patients is also being investigated. For example, the ReGen Collagen Scaffold (Ivy Sports Medicine, formerly ReGen Collagen Scaffold by ReGen Biologics), is a resorbable collagen matrix comprised 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 own 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. For example, Actifit® (Orteq) is a biodegradable polyurethane scaffold that is currently being studied in Europe. Non-absorbable and non-porous synthetic implants for total meniscus replacement are in development. One total meniscus replacement that is in early phase clinical testing is NUsurface® (Active Implants), which is composed of a polyethylene reinforced polycarbonate urethane.

Outcome Measures

The outcomes of this treatment (ie, 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.

REGULATORY STATUS

Collagen Meniscus Implants

In 2008, the ReGen Collagen Scaffold (CS) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. 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 FDA clearance at that time. Amid controversy about this 510(k) clearance decision, FDA reviewed it decision. In October 2010, 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.

POLICY

A. 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:

1. Adult patients should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (eg, younger than 55 years); **AND**

2. Disabling knee pain with activity that is refractory to conservative treatment; **AND**

3. Absence or near absence (more than 50%) of the meniscus, established by imaging or prior surgery; **AND**

4. Documented minimal to absent diffuse degenerative changes in the surrounding articular cartilage (eg, Outerbridge grade II or less, <50% joint space narrowing); **AND**

5. Normal knee biomechanics, or alignment and stability achieved prior to or concurrently with meniscal transplantation.

B. 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:

    1. Autologous chondrocyte implantation; **OR**

    2. Osteochondral allografting; **OR**

    3. Osteochondral autografting.

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

Policy Guidelines

1. 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.
2. Severe obesity, eg, body mass index (BMI) greater than 35 kg/m^2, 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.

RATIONALE

The most recent literature update was performed through February 5, 2018.

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.[4] 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.[5] The analysis found that patients with Outerbridge scores of II or less in any area had significantly improved posttreatment 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).[6] 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

Variables	Elattar et al (2011)[4]	Hergan et al (2011)[5]	Rosso et al (2015)[6]
No. and study type	44 cohort and case series	14 cohort and case series with minimum 2-y follow-up	55 (2 level II, 7 level III, 46 level IV)
Population	1136 knees (1068 patients)	196 knees	1623 patients
Follow-up (range)	4.6 y (8 mo to 20 y)	53.8 mo (24-167 mo)	53.6 mo (12-168 mo)
Outcome measures	Pain and function	Pain and function	Pain and function
Review synthesis			
Pain and function	All showed clinical improvement	Alleviation of knee pain and improvement in function noted	Weighted pre-/postmeasures[a]: VAS pain score decreased from 6.4 to 2.4 LKS increased from 55.5 to 82.7
Failure rate	10.6%	7%-35%	Fresh frozen: 9.9% Cryopreserved: 18.2%
Complication rate	21.3%		10.6%
Review conclusion	MAT improves pain and function	Improvements in objective and subjective outcome measures shown in relatively young patients without significant chondromalacia who underwent concomitant repair for cartilage defects, limb malalignment, and/or limb instability	Agreement in literature on MAT indications: All studies showed clinical improvement at short- and mid-term follow-ups Complication and failure rates acceptable Potential chondro-protective effect of MAT remains unclear
Review limitations	Based primarily on case series	Based primarily on case series and qualitative review only	Based primarily on case series

LKS: Lysholm Knee Score; MAT: meniscal allograft transplantation; VAS: visual analog scale.
[a] Data from 37 of the 55 studies in the systematic review.

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).[7] Another 15 patients who were screened for the RCT decided instead to choose their treatment (referred to as 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.[8] 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).[9]

At a mean follow-up of 16 years, van der Wal et al (2009)[10] reported graft survival decreased to 52.5%, while most failures in the study by Vundelinckx et al (2010)[11] 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

Variables	Verdonk et al (2005)[8]	Van der Wal et al (2009)[10]	Vundelinckx et al (2010)[11]
Sample size	105	57	34/49
Mean age (range), y	35 (16-50)	39 (26-55)	33 (14-47)
Population	Previous total meniscectomy	Previous total meniscectomy	Patients with intact allograft
Intervention	MAT	MAT	MAT
Control	None	None	None
Length of FU (range)	3-15 y	14 y (9-18 y)	105 mo

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

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

Outcomes	Verdonk et al (2005)[8]			Van der Wal et al (2009)[10]			Vundelinckx et al (2010)[11]		
	Base	FU	p	Base	FU	p	Base	FU	p
VAS score							7.0	3.4	<0.001
LKS score				36	61	<0.05	39.7	71.8	<0.001
KOOS score							35.8	60.2	<0.001
Graft survival rate		70%			11 y: 71% 16 y: 52.5%			90%	
Mean survival		11.6 y							

Base: baseline; FU: follow-up; KOOS: Knee Injury and Osteoarthritis Outcome Score; LKS: Lysholm Knee Score; VAS: visual analog scale.

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).[12] 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 4. Summary of Key Systematic Reviews

Variables	Harris et al (2011)[12]
No. and study type	6 case series
Population	110
Intervention	MAT combined with cartilage repair or restoration
Control	Baseline to posttreatment Historical controls of procedures performed in isolation

Variables	Harris et al (2011)[12]
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).[13] Other prospective studies have reported on graft survival and functional outcomes when MAT has been combined with articular cartilage repair.[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^2) and (2) patients with less knee cartilage damage (grade 3b <1 cm^2).[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.[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).[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

Variables	Stone et al (2010)[13]	Kempshall et al (2015)[16]	Ogura et al (2016)[17]	Zaffagnini et al (2016)[18]
Sample size	115	99	17	147
Population	Consecutive patients with grade III-IV chondral damage	Prospective series Grade 3b <1 cm^2 Grade 3b >1 cm^2	Retrospective series	Retrospective series
Intervention	MAT	MACI and microfracture more common if chondral damage was 3c >1 cm^2	ACI with MAT	MAT
Control	None	None	None	None

Variables	Stone et al (2010)[13]	Kempshall et al (2015)[16]	Ogura et al (2016)[17]	Zaffagnini et al (2016)[18]
Outcome measures	MAT survival	MAT survival KOOS, TAS, LKS, IKDC scores	MAT survival MCKRS, WOMAC, VAS, SF-36	MAT survival KOOS, LKS, VAS
Length of FU	5.8 y	2 y	5-10 y	4 y
Results	Mean MAT survival, 9.9 y 47% required additional surgery	Similar outcomes on KOOS, TAS, LKS, IKDC scores for 2 groups MAT survival 97.9% if 3b <1 cm^2 and 78% if 3c >1 cm^2	Mean MAT survival rate, 75% at 5- and 10-y follow-up 67% (12/18) required additional surgery	Mean MAT survival range, 8-9.7 y 17% required additional surgery

ACI: autologous chondrocyte implantation; FU: follow-up; IKDC: International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score; LSK: 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)[19] and the other by Warth et al (2015),[20] are summarized in Table 6. A third, by Zaffagnini et al (2015),[21] 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.[22] No studies in addition to those previously summarized by Warth[20] were cited in this systematic review and Houck is not discussed further.

Table 6. Summary of Key Systematic Reviews for CMI

Variables	Harston et al (2012)[19]	Warth et al (2015)[20]
Search date	May 2011	March 2014
No. of studies	11	13
Population	520	674
Intervention	321 patients received a CMI 41.1% patients had concomitant procedures	439 patients received CMI 32.3% patients had concomitant procedures
Control	Partial meniscectomy alone	
Outcome measures	LKS, TAS, pain scales 8/11 studies provided postoperative imaging data	LKS, TAS, pain scales 11/13 studies provided postoperative imaging data
Length of FU	6-135 mo	3-152 mo

Variables	Harston et al (2012)[19]	Warth et al (2015)[20]
Review synthesis	66%-70% patients receiving CMI had satisfactory outcomes Outcomes in studies with control or comparison groups reported improvements in both groups Reduced CMI size at last follow-up reported in 6 (54.5%) of 11 studies	CMI showed superior clinical outcomes vs partial meniscectomy alone Several studies reported that meniscus scaffold decreased in volume over time 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][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.[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.[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.[26]

Table 7. Summary of Key Study Characteristics for CMI

Variables	Rodkey et al (2008)[23]	Linke et al (2006)[24]	Zaffagnini et al (2011)[25]	Bulgheroni et al 2015)[26]
Study design	RCT	RCT	Controlled cohort	Retrospective cohorts
Sample size	311	60	36	34
Population	Acute and chronic partial meniscectomy		Patient choice	Matched controls

Variables	Rodkey et al (2008)[23]	Linke et al (2006)[24]	Zaffagnini et al (2011)[25]	Bulgheroni et al 2015)[26]
Intervention	CMI	Osteotomy plus CMI	CMI	CMI
Control	Partial meniscectomy alone	Osteotomy alone	Partial meniscectomy alone	Partial meniscectomy alone
Length of FU (range)	59 mo (16-92 mo)	8-18 mo	133 mo (120-152 mo)	9.6 y

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

Table 8. Summary of Key Study Results for CMI

Outcomes	Rodkey et al (2008)[23]			Linke et al (2006)[24]			Zaffagnini et al (2011)[25]			Bulgheroni et al (2015)[26]		
	CMI	Ctrl	p	CMI	Ctrl	p	CMI	Ctrl	p	CMI	Ctrl	p
Survival rate	90%[a]	80% [a]		65%			89%					
VAS pain	19/100[a]	21/100[a]		2.2/10	1.5/10	*NS*	1.2/10	3.3/10	<0.004	14.7/100	13.5/100	*NS*
LKS score	79[a]	78[a]	*NS*	93.6	91.0	*NS*	≈86	≈80	*NS*	94.1	95.5	*NS*
IKDC score						*NS*			<0.001 [b]	85.7	88.1	*NS*
TAS score	42%[a]	29%[a]	<0.02				75	50	<0.026	6 5-6	6 5-6	*NS*

CMI: collagen meniscus implant; Ctrl: control; IKDC: International Knee Documentation Committee; LSK: Lysholm Knee Score; TAS: Tegner Activity Scale; VAS: visual analog scale.

[a] Chronic only.

[b] Higher scores reported by CMI group vs control group.

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. 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 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. 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 1 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 included studies (randomized controlled trials, observational studies) is low. Radiologic evaluations have shown reduced size of the implant in a large portion of patients. The evidence is insufficient to determine the effects of the technology on health outcomes.

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, input was received from 1 physician specialty society (3 reviewers) and 3 academic medical centers while this policy was under review in 2011. The input considered combined meniscal allograft transplantation (MAT) and focal cartilage repair procedures to be medically necessary in 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, input was received from 1 physician specialty society and 3 academic medical centers while this policy was under review 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 with a prior meniscectomy who have disabling knee pain. Contraindications were noted as 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).[2] 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

Statements
Indications for MAT: • Unicompartmental pain post-meniscectomy • In combination with ACL reconstruction when meniscus deficient • In combination with ACR if meniscus deficient

Statements
MAT not recommended for asymptomatic meniscus deficient patient.
Potentially poorer outcomes expected in patients with moderate to severe OA (Kellgren-Lawrence grade ≥3).
Non-irradiated fresh frozen or fresh viable grafts are recommended.
Mechanical axis alignment should be performed prior to MAT; if mechanical axis deviation present, consider realignment osteotomy.
Based on current evidence, superiority of 1 surgical technique over another (all-suture vs bone) is not established.
Outcome scores should include: • Disease-specific: WOMAT • Region-specific: KOOS • Activity: Marx Activity Rating Scale • QOL/utility: EQ-5D

ACL: anterior cruciate ligament; ACR: articular cartilage repair; EQ-5D: EuroQoL 5 dimensions questionnaire; IMREF: International Meniscus Reconstruction Experts Forum; KOOS: Knee injury and Osteoarthritis Outcome Score; MAT: meniscal allograft transplantation; OA: osteoarthritis; QOL: quality of life; WOMAT: Western Ontario Meniscal Evaluation Tool.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Currently ongoing and unpublished trials that might influence this review are listed in Table 12.

Table 12. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01712191[a]	Treatment of the Medial Meniscus with the Treatment of the Medial Meniscus with the NUSurface® Meniscus Implant	150	Jun 2017
NCT01059409	The Clinical and Medico-economical Evaluation of Meniscal Allografts in the Sequelae of Total or Sub-total Meniscectomy	120	Sep 2017
NCT02136901[a]	The VENUS Clinical Study (Verifying the Effectiveness of the NUSurface® System): A Multi-center, Prospective, Randomized, Interventional Superiority Clinical Study	37	Feb 2019

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

CPT/HCPCS

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

G0428 Collagen meniscus implant procedure for filling meniscal defects (e.g., CMI, collagen scaffold, Menaflex)

- There is a CPT category I code specific to this procedure when performed arthroscopically: 29868.

- 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.

ICD-10 Diagnoses

M23.000	Cystic meniscus, unspecified lateral meniscus, right knee
M23.001	Cystic meniscus, unspecified lateral meniscus, left knee
M23.003	Cystic meniscus, unspecified medial meniscus, right knee
M23.004	Cystic meniscus, unspecified medial meniscus, left knee
M23.011	Cystic meniscus, anterior horn of medial meniscus, right knee
M23.012	Cystic meniscus, anterior horn of medial meniscus, left knee
M23.021	Cystic meniscus, posterior horn of medial meniscus, right knee
M23.022	Cystic meniscus, posterior horn of medial meniscus, left knee
M23.031	Cystic meniscus, other medial meniscus, right knee
M23.032	Cystic meniscus, other medial meniscus, left knee
M23.041	Cystic meniscus, anterior horn of lateral meniscus, right knee
M23.042	Cystic meniscus, anterior horn of lateral meniscus, left knee
M23.051	Cystic meniscus, posterior horn of lateral meniscus, right knee
M23.052	Cystic meniscus, posterior horn of lateral meniscus, left knee
M23.061	Cystic meniscus, other lateral meniscus, right knee
M23.062	Cystic meniscus, other lateral meniscus, left knee
M23.200	Derangement of unspecified lateral meniscus due to old tear or injury, right knee
M23.201	Derangement of unspecified lateral meniscus due to old tear or injury, left knee
M23.203	Derangement of unspecified medial meniscus due to old tear or injury, right knee
M23.204	Derangement of unspecified medial meniscus due to old tear or injury, left knee
M23.206	Derangement of unspecified meniscus due to old tear or injury, right knee
M23.207	Derangement of unspecified meniscus due to old tear or injury, left knee
M23.211	Derangement of anterior horn of medial meniscus due to old tear or injury, right knee
M23.212	Derangement of anterior horn of medial meniscus due to old tear or injury, left knee
M23.221	Derangement of posterior horn of medial meniscus due to old tear or injury, right knee
M23.222	Derangement of posterior horn of medial meniscus due to old tear or injury, left knee
M23.231	Derangement of other medial meniscus due to old tear or injury, right knee
M23.232	Derangement of other medial meniscus due to old tear or injury, left knee
M23.241	Derangement of anterior horn of lateral meniscus due to old tear or injury, right knee
M23.242	Derangement of anterior horn of lateral meniscus due to old tear or injury, left knee
M23.251	Derangement of posterior horn of lateral meniscus due to old tear or injury, right knee

M23.252	Derangement of posterior horn of lateral meniscus due to old tear or injury, left knee
M23.261	Derangement of other lateral meniscus due to old tear or injury, right knee
M23.262	Derangement of other lateral meniscus due to old tear or injury, left knee
M23.300	Other meniscus derangements, unspecified lateral meniscus, right knee
M23.301	Other meniscus derangements, unspecified lateral meniscus, left knee
M23.304	Other meniscus derangements, unspecified medial meniscus, left knee
M23.306	Other meniscus derangements, unspecified meniscus, right knee
M23.307	Other meniscus derangements, unspecified meniscus, left knee
M23.311	Other meniscus derangements, anterior horn of medial meniscus, right knee
M23.312	Other meniscus derangements, anterior horn of medial meniscus, left knee
M23.321	Other meniscus derangements, posterior horn of medial meniscus, right knee
M23.322	Other meniscus derangements, posterior horn of medial meniscus, left knee
M23.331	Other meniscus derangements, other medial meniscus, right knee
M23.332	Other meniscus derangements, other medial meniscus, left knee
M23.341	Other meniscus derangements, anterior horn of lateral meniscus, right knee
M23.342	Other meniscus derangements, anterior horn of lateral meniscus, left knee
M23.351	Other meniscus derangements, posterior horn of lateral meniscus, right knee
M23.352	Other meniscus derangements, posterior horn of lateral meniscus, left knee
M23.361	Other meniscus derangements, other lateral meniscus, right knee
M23.362	Other meniscus derangements, other lateral meniscus, left knee
Q68.6	Discoid meniscus
S83.200A	Bucket-handle tear of unspecified meniscus, current injury, right knee, initial encounter
S83.200D	Bucket-handle tear of unspecified meniscus, current injury, right knee, subsequent encounter
S83.200S	Bucket-handle tear of unspecified meniscus, current injury, right knee, sequela
S83.201A	Bucket-handle tear of unspecified meniscus, current injury, left knee, initial encounter
S83.201D	Bucket-handle tear of unspecified meniscus, current injury, left knee, subsequent encounter
S83.201S	Bucket-handle tear of unspecified meniscus, current injury, left knee, sequela
S83.203A	Other tear of unspecified meniscus, current injury, right knee, initial encounter
S83.203D	Other tear of unspecified meniscus, current injury, right knee, subsequent encounter
S83.203S	Other tear of unspecified meniscus, current injury, right knee, sequela
S83.204A	Other tear of unspecified meniscus, current injury, left knee, initial encounter
S83.204D	Other tear of unspecified meniscus, current injury, left knee, subsequent encounter
S83.204S	Other tear of unspecified meniscus, current injury, left knee, sequela
S83.206A	Unspecified tear of unspecified meniscus, current injury, right knee, initial encounter
S83.206D	Unspecified tear of unspecified meniscus, current injury, right knee, subsequent encounter
S83.206S	Unspecified tear of unspecified meniscus, current injury, right knee, sequela
S83.207A	Unspecified tear of unspecified meniscus, current injury, left knee, initial encounter

S83.207D Unspecified tear of unspecified meniscus, current injury, left knee, subsequent encounter
S83.207S Unspecified tear of unspecified meniscus, current injury, left knee, sequela
S83.211A Bucket-handle tear of medial meniscus, current injury, right knee, initial encounter
S83.211D Bucket-handle tear of medial meniscus, current injury, right knee, subsequent encounter
S83.211S Bucket-handle tear of medial meniscus, current injury, right knee, sequela
S83.212A Bucket-handle tear of medial meniscus, current injury, left knee, initial encounter
S83.212D Bucket-handle tear of medial meniscus, current injury, left knee, subsequent encounter
S83.212S Bucket-handle tear of medial meniscus, current injury, left knee, sequela
S83.221A Peripheral tear of medial meniscus, current injury, right knee, initial encounter
S83.221D Peripheral tear of medial meniscus, current injury, right knee, subsequent encounter
S83.221S Peripheral tear of medial meniscus, current injury, right knee, sequela
S83.222A Peripheral tear of medial meniscus, current injury, left knee, initial encounter
S83.222D Peripheral tear of medial meniscus, current injury, left knee, subsequent encounter
S83.222S Peripheral tear of medical meniscus, current injury, left knee, sequela
S83.231A Complex tear of medial meniscus, current injury, right knee, initial encounter
S83.231D Complex tear of medial meniscus, current injury, right knee, subsequent encounter
S83.231S Complex tear of medial meniscus, current injury, right knee, sequela
S83.232A Complex tear of medial meniscus, current injury, left knee, initial encounter
S83.232D Complex tear of medial meniscus, current injury, left knee, subsequent encounter
S83.232S Complex tear of medial meniscus, current injury, left knee, sequela
S83.241A Other tear of medial meniscus, current injury, right knee, initial encounter
S83.241D Other tear of medial meniscus, current injury, right knee, subsequent encounter
S83.241S Other tear of medial meniscus, current injury, right knee, sequela
S83.242A Other tear of medial meniscus, current injury, left knee, initial encounter
S83.242D Other tear of medial meniscus, current injury, left knee, subsequent encounter
S83.242S Other tear of medial meniscus, current injury, left knee, sequela
S83.251A Bucket-handle tear of lateral meniscus, current injury, right knee, initial encounter
S83.251D Bucket-handle tear of lateral meniscus, current injury, right knee, subsequent encounter
S83.251S Bucket-handle tear of lateral meniscus, current injury, right knee, sequela
S83.252A Bucket-handle tear of lateral meniscus, current injury, left knee, initial encounter
S83.252D Bucket-handle tear of lateral meniscus, current injury, left knee, subsequent encounter
S83.252S Bucket-handle tear of lateral meniscus, current injury, left knee, sequela
S83.261A Peripheral tear of lateral meniscus, current injury, right knee, initial encounter

S83.261D	Peripheral tear of lateral meniscus, current injury, right knee, subsequent encounter
S83.261S	Peripheral tear of lateral meniscus, current injury, right knee, sequela
S83.262A	Peripheral tear of lateral meniscus, current injury, left knee, initial encounter
S83.262D	Peripheral tear of lateral meniscus, current injury, left knee, subsequent encounter
S83.262S	Peripheral tear of lateral meniscus, current injury, left knee, sequela
S83.271A	Complex tear of lateral meniscus, current injury, right knee, initial encounter
S83.271D	Complex tear of lateral meniscus, current injury, right knee, subsequent encounter
S83.271S	Complex tear of lateral meniscus, current injury, right knee, sequela
S83.272A	Complex tear of lateral meniscus, current injury, left knee, initial encounter
S83.272D	Complex tear of lateral meniscus, current injury, left knee, subsequent encounter
S83.272S	Complex tear of lateral meniscus, current injury, left knee, sequela
S83.281A	Other tear of lateral meniscus, current injury, right knee, initial encounter
S83.281D	Other tear of lateral meniscus, current injury, right knee, subsequent encounter
S83.281S	Other tar of lateral meniscus, current injury, right knee, sequela
S83.282A	Other tear of lateral meniscus, current injury, left knee, initial encounter
S83.282D	Other tear of lateral meniscus, current injury, left knee, subsequent encounter
S83.282S	Other tear of lateral meniscus, current injury, left knee, sequela
S83.31XA	Tear of articular cartilage of right knee, current, initial encounter
S83.31XD	Tear of articular cartilage of right knee, current, subsequent encounter
S83.31XS	Tear of articular cartilage of right knee, current, sequela
S83.32XA	Tear of articular cartilage of left knee, current, initial encounter
S83.32XD	Tear of articular cartilage of left knee, current, subsequent encounter
S83.32XS	Tear of articular cartilage of left knee, current, sequela

REVISIONS

07-21-2011	Updated the Description section.
	In the Policy section: ▪ Removed "Meniscal transplantation is experimental / investigational due to the lack of long-term studies." ▪ Added: A. 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 the following criteria are met: 1. 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). 2. Disabling knee pain wit activity that is refractory to conservative treatment. 3. Absence or near absence (more than 50%) of the meniscus, established by imaging or prior surgery. 4. Documentation minimal to absent diffuse degenerative changes in the surrounding articular cartilage (e.g., Outerbridge grade II or less, < 50% joint space narrowing).

	5. Normal knee biomechanics, or alignment and stability achieved concurrently with Meniscal transplantation. B. Meniscal allograft transplantation may be considered medically necessary when performed in combination, either concurrently or sequentially, with autologous chondrocyte implantation, osteochondral allografting or osteochondral autografting for focal articular cartilage lesions. C. Collagen meniscus implants are considered experimental / investigational. Policy Guidelines Patients should exhibit symptoms of persistent disabling knee pain that has not shown an adequate response 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 (BMI) 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 a total knee arthroplasty.
	Added Rationale section.
	In the Diagnosis section: ▪ Added 717.1-717.5; 836.0-836.2
	Added Revisions section.
	Added Reference section.
08-13-2012	Rationale section updated.
	Reference section updated.
09-17-2013	In the Medical Policy Title, replaced "collagen" with "other" to read "Meniscal Allografts and Other Meniscus Implants"
	Updated Description section.
	In Policy section: ▪ In Item C, replaced "collagen" with "Use of" to read "Use of other meniscal implants…"
	Updated Rationale section.
	In Coding section: ▪ Updated coding nomenclature. ▪ Added HCPCS code G0428. ▪ Added ICD-10 Diagnosis codes. *(Effective October 1,2 014)*
	Reference section updated.
03-04-2015	In Policy section: ▪ In Item A #5, added "prior to or", to read, "Normal knee biomechanics, or alignment and stability achieved prior to or concurrently with meniscal transplantation." ▪ In item B, added "treatment of focal articular cartilage lesions using any of the following procedures:" to read, "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:" ▪ In item B #1, removed "for focal articular cartilage lesions", to read, "Osteochondral autografting." ▪ In Item C, added "incorporating materials such as collagen and polyurethane are," to read, "Use of other meniscal implants incorporating materials such as collagen and polyurethane are considered experimental / investigational."
	Updated Rationale section.
	In Coding section:

	▪ In CPT/HCPCS bullet points, removed ",G0428 –collagen meniscus implant procedure for filling meniscal defect (e.g., CMI, collagen scaffold, Menaflex)," to read, "There is no CPT code for implantation of the ReGen Collagen Scaffold but the American Academy of Orthopedic Surgeons' …"
	Updated References section.
05-13-2015	Updated Rationale section.
	Updated References section.
05-24-2017	Updated Description section.
	Updated Rationale section.
	Updated References section.
05-23-2018	Updated Description section.
	In Policy section: ▪ Updated Policy Guidelines.
	Updated Rationale section.
	In Coding section: ▪ Updated coding bullets. ▪ Removed ICD-9 codes.
	Updated References section.

REFERENCES

1. Cvetanovich GL, Yanke AB, McCormick F, et al. Trends in meniscal allograft transplantation in the United States, 2007 to 2011. *Arthroscopy.* Jun 2015;31(6):1123-1127. PMID 25682330
2. Getgood A, LaPrade RF, Verdonk P, et al. International Meniscus Reconstruction Experts Forum (IMREF) 2015 consensus statement on the practice of meniscal allograft transplantation. *Am J Sports Med.* Aug 25 2017;45(5):1195-1205. PMID 27562342
3. Frank RM, Cole BJ. Meniscus transplantation. *Curr Rev Musculoskelet Med.* Dec 2015;8(4):443-450. PMID 26431702
4. Elattar M, Dhollander A, Verdonk R, et al. Twenty-six years of meniscal allograft transplantation: is it still experimental? A meta-analysis of 44 trials. *Knee Surg Sports Traumatol Arthrosc.* Feb 2011;19(2):147-157. PMID 21161170
5. Hergan D, Thut D, Sherman O, et al. Meniscal allograft transplantation. *Arthroscopy.* Jan 2011;27(1):101-112. PMID 20884166
6. Rosso F, Bisicchia S, Bonasia DE, et al. Meniscal allograft transplantation: a systematic review. *Am J Sports Med.* Apr 2015;43(4):998-1007. PMID 24928760
7. Smith NA, Parsons N, Wright D, et al. A pilot randomized trial of meniscal allograft transplantation versus personalized physiotherapy for patients with a symptomatic meniscal deficient knee compartment. *Bone Joint J.* Jan 2018;100-B(1):56-63. PMID 29305451
8. Verdonk PC, Demurie A, Almqvist KF, et al. Transplantation of viable meniscal allograft. Survivorship analysis and clinical outcome of one hundred cases. *J Bone Joint Surg Am.* Apr 2005;87(4):715-724. PMID 15805198
9. Hommen JP, Applegate GR, Del Pizzo W. Meniscus allograft transplantation: ten-year results of cryopreserved allografts. *Arthroscopy.* Apr 2007;23(4):388-393. PMID 17418331
10. van der Wal RJ, Thomassen BJ, van Arkel ER. Long-term clinical outcome of open meniscal allograft transplantation. *Am J Sports Med.* Nov 2009;37(11):2134-2139. PMID 19542303
11. Vundelinckx B, Bellemans J, Vanlauwe J. Arthroscopically assisted meniscal allograft transplantation in the knee: a medium-term subjective, clinical, and radiographical outcome evaluation. *Am J Sports Med.* Nov 2010;38(11):2240-2247. PMID 20724642
12. 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.* Mar 2011;27(3):409-418. PMID 21030203

13. Stone KR, Adelson WS, Pelsis JR, et al. Long-term survival of concurrent meniscus allograft transplantation and repair of the articular cartilage: a prospective two- to 12-year follow-up report. *J Bone Joint Surg Br.* Jul 2010;92(7):941-948. PMID 20595111
14. Farr J, Rawal A, Marberry KM. Concomitant meniscal allograft transplantation and autologous chondrocyte implantation: minimum 2-year follow-up. *Am J Sports Med.* Sep 2007;35(9):1459-1466. PMID 17435058
15. Rue JP, Yanke AB, Busam ML, et al. Prospective evaluation of concurrent meniscus transplantation and articular cartilage repair: minimum 2-year follow-up. *Am J Sports Med.* Sep 2008;36(9):1770-1778. PMID 18483199
16. Kempshall PJ, Parkinson B, Thomas M, et al. Outcome of meniscal allograft transplantation related to articular cartilage status: advanced chondral damage should not be a contraindication. *Knee Surg Sports Traumatol Arthrosc.* Jan 2015;23(1):280-289. PMID 25432522
17. Ogura T, Bryant T, Minas T. Biological knee reconstruction with concomitant autologous chondrocyte implantation and meniscal allograft transplantation: mid- to long-term outcomes. *Orthop J Sports Med.* Oct 2016;4(10):2325967116668490. PMID 27803938
18. Zaffagnini S, Grassi A, Marcheggiani Muccioli GM, et al. Survivorship and clinical outcomes of 147 consecutive isolated or combined arthroscopic bone plug free meniscal allograft transplantation. *Knee Surg Sports Traumatol Arthrosc.* May 2016;24(5):1432-1439. PMID 26860105
19. Harston A, Nyland J, Brand E, et al. Collagen meniscus implantation: a systematic review including rehabilitation and return to sports activity. *Knee Surg Sports Traumatol Arthrosc.* Jan 2012;20(1):135-146. PMID 21695465
20. Warth RJ, Rodkey WG. Resorbable collagen scaffolds for the treatment of meniscus defects: a systematic review. *Arthroscopy.* May 2015;31(5):927-941. PMID 25595693
21. Zaffagnini S, Grassi A, Marcheggiani Muccioli GM, et al. MRI evaluation of a collagen meniscus implant: a systematic review. *Knee Surg Sports Traumatol Arthrosc.* Nov 2015;23(11):3228-3237. PMID 24993568
22. Houck DA, Kraeutler MJ, Belk JW, et al. Similar clinical outcomes following collagen or polyurethane meniscal scaffold implantation: a systematic review. *Knee Surg Sports Traumatol Arthrosc.* Jan 16 2018. PMID 29340746
23. Rodkey WG, DeHaven KE, Montgomery WH, 3rd, et al. Comparison of the collagen meniscus implant with partial meniscectomy. A prospective randomized trial. *J Bone Joint Surg Am.* Jul 2008;90(7):1413-1426. PMID 18594088
24. Linke RD, Ulmer M, Imhoff AB. [Replacement of the meniscus with a collagen implant (CMI)] [German]. *Oper Orthop Traumatol.* Dec 2006;18(5-6):453-462. PMID 17171330
25. Zaffagnini S, Marcheggiani Muccioli GM, Lopomo N, et al. Prospective long-term outcomes of the medial collagen meniscus implant versus partial medial meniscectomy: a minimum 10-year follow-up study. *Am J Sports Med.* May 2011;39(5):977-985. PMID 21297005
26. Bulgheroni E, Grassi A, Bulgheroni P, et al. Long-term outcomes of medial CMI implant versus partial medial meniscectomy in patients with concomitant ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc.* Nov 2015;23(11):3221-3227. PMID 24990662
27. National Institute for Health and Care Excellence (NICE). Partial replacement of the meniscus of the knee using a biodegradable scaffold: guidance [IPG430]. 2012; https://www.nice.org.uk/guidance/IPG430. Accessed March 16, 2018.
28. American Academy of Orthopaedic Surgeons. OrthoInfo: Meniscal transplant surgery. 2014; https://orthoinfo.aaos.org/en/treatment/meniscal-transplant-surgery/. Accessed March 16, 2018.
29. Centers for Medicare and Medicaid Services (CMS). Decision Memo for COLLAGEN MENISCUS IMPLANT (CAG-00414N). 2010; https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=235&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=Collagen+Meniscus+Implant&KeyWordLookUp=Title&KeyWordSearchType=And&id=235&bc=gAAAACAACAAAAA%3d%3d&. Accessed March 16, 2018.

Other References

1. Blue Cross and Blue Shield of Kansas, Orthopedic Liaison Committee, January 2007; February 2013; February 2015; June 2016.
2. Blue Cross and Blue Shield of Kansas, Medical Advisory Committee, April 2007.
3. Blue Cross and Blue Shield of Kansas, Orthopedic Liaison Committee, CB, May 2011.