Menaflex

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers the Menaflex device (previously known as the Collagen Meniscal Implant and the Collagen Scaffold device) experimental and investigational for repair and reinforcement of the medial meniscus of the knee and all other indications because of insufficient evidence of its effectiveness.


Background

The menisci of the knee are semi-lunar fibrocartilaginous structures critical in load bearing, shock absorption, stability, and lubrication. Loss of meniscal tissue can lead to pain, decreased function and activity. Current methods of treating repairable meniscal tears include standard
Suture, meniscal tacks, darts, and arrow devices. Patients with meniscal tears that cannot be repaired by these methods typically receive partial or total meniscectomy. However, several investigators believe that degenerative processes in adjacent articular cartilage surfaces may be associated with partial or total meniscectomy and could influence knee function over time (Hede et al, 1992; Schimmer et al, 1998).

Allografts or synthetic meniscus scaffolds have been used for meniscus tears to prevent early degenerative joint disease with varying success, although problems related to reduced initial and long-term stability, as well as immunological reactions prevent wide-spread clinical use (Sandmann et al, 2009).

Collagen meniscus implants, also known as collagen scaffolds or Menaflex, are implantable porous meniscus scaffolds composed of collagen fibers, enriched with glycosaminoglycan, used as a template and support for generation of new tissue to replace the lost menisci.

In December 2008, Menaflex (ReGen Biologics, Inc., Hackensack, NJ), previously known as collagen meniscus implant (CMI), received U.S. Food and Drug Administration (FDA) 510(k) marketing clearance as a collagen scaffold for repair and reinforcement of the medial meniscus of the knee. It is a synthetic resorbable collagen matrix implant comprised of bovine type I collagen and is intended for the reinforcement and repair of soft tissue injuries of the medial meniscus where weakness exists, such as defects that result from prior surgeries to the involved meniscus (e.g., partial meniscectomy). The implant is a crescent-shaped device that can be trimmed to fit the defect in the meniscal tissue and is sutured to the remaining native meniscus during arthroscopic surgery. The device provides a sponge-like scaffold that is replaced by the patient's own meniscal tissue over time.

In its 510(k) submission, the manufacturer provided the FDA with data from a prospective, randomized, controlled, multi-center study that compared the Menaflex with partial meniscectomy. Patients (n = 311) with an irreparable injury of the medial meniscus or a previous partial medial meniscectomy were enrolled in the study. There were 2 study arms: (i) patients (n = 157) with no prior surgery on the involved meniscus (the "acute" arm of the study), and (ii) patients (n = 154) with prior (1 to 3) meniscal surgical procedures (the "chronic" arm).

Patients were randomized either to receive the collagen meniscus implant or to serve as a control subject treated with a partial meniscectomy only. Subjects underwent frequent clinical follow-up examinations over 2 years and completed validated outcomes questionnaires over 7 years. Patients who had received a collagen meniscus implant were required by protocol to have second-look arthroscopy at 1 year to determine the amount of new tissue growth and to perform a biopsy to assess tissue quality. Re-operation and survival rates were determined. In
the acute group, 75 patients received a collagen meniscus implant and 82 were controls. In the chronic group, 85 patients received the implant and 69 were controls. The mean duration of follow-up was 59 months (range of 16 to 92 months). The 141 repeat arthroscopies done at 1 year showed that the collagen meniscus implants had resulted in significantly (p = 0.001) increased meniscal tissue compared with that seen after the original index partial meniscectomy. The implant supported meniscus-like matrix production and integration as it was assimilated and resorbed. In the chronic group, patients who had received an implant regained significantly more of their lost activity than did controls (p = 0.02) and they underwent significantly fewer non-protocol re-operations (p = 0.04). No differences were detected between the 2 treatment groups in the acute arm of the study. Of the 12 documented serious complications in patients with the Menaflex, 7 were classified as probably or at least possibly related to the Menaflex. In 1 patient, a skin infection developed at a portal site requiring joint irrigation and debridement and the Menaflex was removed. Pain scores, Lysholm scores, and patient self-assessment scores improved between the pre-operative and latest follow-up evaluations in all treatment groups and were similar regardless of treatment or chronicity. The authors concluded that the Menaflex device supports new tissue ingrowth and that the new tissue ingrowth is adequate to enhance meniscal function in patients with a chronic meniscal injury; however, it does not have any benefit for patients with an acute injury (Rodkey et al, 2008).

It is interesting to note that the FDA (2008) made the following observations during their analysis of the Rodkey study data: (i) the majority of the Menaflex devices were firmly attached to the host rim, however, 16 % were not firmly attached and 18 % of knee compartments were determined to be worse than during the operative procedure at the time of the re-look arthroscopic procedure, (ii) the investigators reported that 5 years after receiving a Menaflex implant, 22.7 % of control patients required further meniscal surgery, compared to only 9.5 % of the Menaflex recipients, however, if additional operations that were performed during the second arthroscopy are included, the re-operation rate among Menaflex recipients was 19.7 %, and (iii) the Tegner Index is meant to complement other functional scores (e.g., the Lysholm knee score) for patients with ligamentous injuries, however, the investigators reported the Tegner Index in isolation and there was no pre-specified hypothesis for its use in the study design, thus, it is unclear how this endpoint should be interpreted given that there is no defined clinical significance for the Tegner Score when used in isolation. In addition, there is a noted difference in the rehabilitation necessary for individuals receiving the Menaflex implant versus partial meniscectomy. During the first 6 months following implantation, the patient's activity level is restricted to reduce the stress on the mesh-reinforced meniscus, allowing tissue in-growth and maturation to take place. In contrast, the rehabilitation program for a partial meniscectomy is to return to full activities by 2 to 3 weeks post-operatively since there is no period of meniscal healing required.
At the 75th annual meeting of the American Academy of Orthopaedic Surgeons in March 2008, histologic findings were presented from patients who had received the Menaflex implant (n = 128). Biopsies taken 1 year after implantation found residual implant material in 63 % of cases and all cases showed infiltration of the implant matrix with new meniscal tissue. Inflammation was noted around the implant in 9 % of patients (Choi, 2008).

Systematic evidence reviews have not evaluated the Menaflex device. A Cochrane review (Howell and Handoll, 2000) on the effects of common surgical interventions in the treatment of meniscal injuries of the knee concluded, "[t]he lack of randomised trials means that no conclusions can be drawn on the issue of surgical versus non-surgical treatment of meniscal injuries, nor meniscal tear repair versus excision. In randomised trials so far reported, there is no evidence of difference in radiological or long term clinical outcomes between arthroscopic and open meniscal surgery, or between total and partial meniscectomy. Partial meniscectomyseems preferable to the total removal of the meniscus in terms of recovery and overall functional outcome in the short term."

Although some clinical studies have demonstrated improvement with the collagen meniscus implant, the number of patients have been small in all studies and the positive effect on the prevention of progression of osteoarthritis was not compared with control groups (Bumam, 2007).

An assessment by the California Technology Assessment Forum (Tice, 2010) concluded that the collagen meniscus implant does not meet CTAF criteria. The CTAF assessment found that the pivotal randomized clinical trial (citing Rodkey et al, 2008) failed to demonstrate any improvement in pain or symptoms in either arm of the trial and the trial has substantial risk for selection bias, confounding, and reporting bias because of the large number of patients lost to follow-up after randomization and the lack of blinding for subjective outcomes. In addition, no data on osteoarthritis were presented. The CTAF assessment concluded that the trial "presents evidence that the collagen meniscus implant offers no important clinical benefits, requires longer and more intensive post-operative rehabilitation, and some uncertainty remains about the potential for long-term harm from the device."

The Centers for Medicare and Medicaid Services (CMS, 2010) has concluded that the collagen meniscus implant does not improve health outcomes in the Medicare population. Therefore, CMS has determined that the collagen meniscus implant is not reasonable and necessary for the treatment of meniscal injury/tear. Furthermore, on October 14, 2010, the FDA announced that the Menaflex Collagen Scaffold should not have been cleared for marketing in the United States. The FDA has now concluded that the Menaflex device is intended to be used for different purposes and is technologically dissimilar from devices already on the market known...
as “predicate devices”. These differences can affect the safety and effectiveness of the Menaflex device. For example, instead of simply repairing or reinforcing damaged tissue like predicate devices, Menaflex is intended to stimulate the growth of new tissue to replace tissue that was surgically removed. Because of these differences, the Menaflex device should not have been cleared by the agency. The announcement follows a re-evaluation of the scientific evidence that was undertaken after a September 2009 agency report identified problems in the agency's review of the device. To correct this error, the agency will begin the process to rescind the product's marketing clearance.

In a case-series study, Monllau et al (2011) evaluated the clinical outcome of a collagen meniscus implant (CMI) in an injured medial meniscus after a minimum of 10 years' follow-up. A total of 25 patients underwent arthroscopic CMI. They had either persistent compartmental joint line pain due to a previous medial meniscus resection (5 cases) or a large irreparable meniscus tear at arthroscopy (20 cases). Implant failure was defined as infection due to the implant or mechanical failure of the device. Twenty-two patients returned for clinical, functional, and radiographic evaluation. Magnetic resonance imaging was also performed and was analyzed with the criteria of Genovese et al (where type 3 indicates normal and type 1 indicates completely abnormal). All the afore-mentioned evaluations were carried out at a minimum of 10 years (range of 10.1 to 12.5 years) after the procedure. The mean Lysholm score improved from 59.9 pre-operatively to 89.6 at 1 year (p < 0.001), and it was 87.5 at final follow-up (p < 0.001). The results were good or excellent in 83% of the population. No differences were observed between the Lysholm score at 1 year of follow-up with the score at final follow-up (p > 0.05). The mean pain score on a visual analog scale (VAS) improved by 3.5 points at final follow-up. Patient satisfaction with the procedure was 3.4 of 4 points. Radiographic evaluation showed either minimal or no narrowing of the joint line. Magnetic resonance imaging showed type 2 in 64% of cases and type 3 in 21%. All cases showed less volume than expected (size type 2 in 89%). The failure rate in the patient population was 8% (2 of 25). There were no complications related to the device. The authors concluded that although there were several different types of patients and acute and chronic tears were treated in a limited number of patients, meniscal substitution with CMI provides significant pain relief and functional improvement after a minimum of 10 years' follow-up. The implant generally diminished in size, but the procedure proved to be safe and had a low rate of implant failure on a long-term basis. No development or progression of degenerative knee joint disease was observed in most cases (Level IV evidence).

In a cohort study, Zaffagnini et al (2011) compared the long-term outcomes of the medial collagen meniscus implant (MCMI) versus partial medial meniscectomy (PMM). A total of 33 non-consecutive patients (men; mean age of 40 years) with meniscal injuries were enrolled in the study to receive MCMI or to serve as a control patient treated with PMM. The choice of
treatment was decided by the patient. All patients were clinically evaluated at time 0 and at 5 years and a minimum of 10 years after surgery (mean follow-up of 133 months) by Lysholm, VAS for pain, objective International Knee Documentation Committee (IKDC) knee form, and Tegner activity level scores. The SF-36 score was performed pre-operatively and at final follow-up. Bilateral weight-bearing radiographs were completed before the index surgery and at final follow-up. Minimum 10-year follow-up MRI images were compared with pre-operative MRI images by means of the Yulish score. The Genovese score was also used to evaluate MCMI MRI survivorship. The MCMI group, compared with the PMM group, showed significantly lower VAS for pain (1.2 +/- 0.9 versus 3.3 +/- 1.8; p = 0.004) and higher objective IKDC (7A and 10B for MCMI, 4B and 12C for PMM; p = 0.0001), Teger index (75 +/- 27.5 versus 50 +/- 11.67; p = 0.026), and SF-36 (53.9 +/- 4.0 versus 44.1 +/- 9.2; p = 0.026 for Physical Health Index; 54.7 +/- 3.8 versus 43.8 +/- 6.5; p = 0.004 for Mental Health Index) scores. Radiographic evaluation showed significantly less medial joint space narrowing in the MCMI group than in the PMM group (0.48 +/- 0.63 mm versus 2.13 +/- 0.79 mm; p = 0.0003). No significant differences between groups were reported regarding Lysholm (p = 0.062) and Yulish (p = 0.122) scores. Genovese score remained constant between 5 and 10 years after surgery (p = 0.5). The MRI evaluation of the MCMI patients revealed 11 cases of myxoid degeneration signal: 4 had a normal signal with reduced size, and 2 had no recognizable implant. The authors concluded that pain, activity level, and radiological outcomes are significantly improved with use of the MCMI at a minimum 10-year follow-up compared with PMM alone. Moreover, they stated that randomized controlled trials on a larger population are needed to confirm MCMI benefits at long-term.

Harston et al (2012) examined CMI effectiveness for improving patient function, symptoms, and activity level. Study methodologies, rehabilitation, and return to sports guidelines were also reviewed. MedLine, EMBASE, CINAHL, Life Science Citations, and Cochrane Central Register of Controlled Trials databases were searched from January 1995 to May 2011 using the term collagen meniscal or meniscus implant. Only human studies with English language abstracts that reported patient outcomes were included. Modified Coleman Methodology criteria were used to score research quality. A total of 11 studies with 520 subjects (men = 428; women = 92; 17.7 % women) of 38.2 +/- 3.7 years of age met the inclusion criteria. Of these subjects, 321 (men = 263, women = 58; 18.1 % women) received a CMI. Based primarily on Lysholm Knee Score, Tegner Activity Scale, pain scales and self-assessment measurements knee function, symptoms, and activity level generally improved by 46.6 +/- 39.9 months post-surgery. Rehabilitation was described in 9/11 (81.8 %) studies and 4 released patients to full activities at 6 months post-surgery. No study described how advanced rehabilitation or function testing contributed to return to activity decision-making. Research quality was generally low (67.1 +/- 18.6) with widely ranging (29 to 97) scores. Reduced CMI size at last follow-up was reported in 6/11 (54.5 %) studies, but the significance of this finding is unknown. The authors concluded that knee function, symptoms, and activity level generally improved following CMI use, but poor
research report quality was common. They stated that additional well-designed long-term prospective studies are needed to better determine knee osteoarthritis prevention efficacy and appropriate patient selection.

Furthermore, the Work Loss Data Institute's guideline on "Knee and leg (acute and chronic)" (2011; updated November 2013) does not recommend the use of CMI/Menaflex.

Spencer et al (2012) presented their early experience on meniscal scaffolds and performed a review of the literature. A total of 23 patients underwent meniscal scaffold implantation (14 medial, 9 lateral) with either the Menaflex (ReGen Biologics) (n = 12) or Actifit (Orteq) (n = 11) scaffolds. Minimum follow-up was 1 year with a mean of 24.1 months (18 to 27) for the Menaflex and 14.7 months (12 to 18) for the Actifit groups. Mean age at surgery was 35 years (17 to 47) with a mean Outerbridge grade of 1.9 in the affected compartment. Eight (36%) underwent concurrent osteotomy, ligament reconstruction or microfracture of the tibial plateau. KOOS, Lysholm, Tegner activity and IKDC scores were collected pre-operatively and at 6-month interval post-surgery. Assessment of the reconstruction was obtained with MRI scanning and arthroscopy. One scaffold tore and was revised at 19 months post-operatively. A total of 21 out of 23 (91.3%) had a significant improvement in knee scores when compared to pre-surgery levels at latest follow-up. Second-look arthroscopy in 14 at 1-year post-implantation showed variable amounts of regenerative tissue. There was no progression in chondral wear noted on repeat MRI scanning. The authors concluded that treatment with meniscal scaffold implants can provide good pain relief for the post-meniscectomy knee following partial meniscectomy. Moreover, they stated that longer follow-up is needed to examine if they also prevent the progressive chondral wear associated with a post-meniscectomy knee.

The National Institute for Health and Clinical Excellence's guideline on "Partial replacement of the meniscus of the knee using a biodegradable scaffold" (NICE, 2012) states that "Current evidence on partial replacement of the meniscus of the knee using a biodegradable scaffold raises no major safety concerns. Evidence for any advantage of the procedure over standard surgery, for symptom relief in the short-term, or for any reduction in further operations in the long-term, is limited in quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research".

Brophy and Matava (2012) stated that as a result of biologic issues and technical limitations, repair of the meniscus is indicated for unstable, peripheral vertical tears; most other types of meniscal tears that are degenerative, significantly traumatized, and/or located in an avascular area of the meniscus are managed with partial meniscectomy. Options to restore the meniscus range from allograft transplantation to the use of synthetic technologies. Recent studies demonstrated good long-term outcomes from meniscal allograft transplantation, although the
indications and techniques continue to evolve and the long-term chondro-protective potential has yet to be determined. Several synthetic implants, none of which has FDA approval, have shown some promise for replacing part or all of the meniscus, including the collagen meniscal implant, hydrogels, and polymer scaffolds.

Papalia et al (2013) systematically reviewed the literature on clinical outcomes following partial meniscal replacement using different scaffolds. These investigators performed a comprehensive search of Medline, CINAHL, Embase and the Cochrane Central Registry of Controlled Trials. The reference lists of the selected articles were then examined by hand. Only studies focusing on investigation of clinical outcomes on patients undergoing a partial meniscal replacement using a scaffold were selected. These researchers then evaluated the methodological quality of each article using the Coleman methodologyscore (CMS), a 10-criteria scoring list assessing the methodological quality of the selected studies (CMS). A total of 15 studies were included, all prospective studies, but only 2 were randomized controlled trials (RCTs). Biological scaffolds were involved in 12 studies, 2 studies investigated synthetic scaffolds, whereas 1 remaining article presented data from the use of both classes of device. The mean modified CMS was 64.6. Several demographic and biomechanical factors could influence the outcomes of this treatment modality. Partial replacement using both classes of scaffolds achieved significant and encouraging improved clinical results when compared with baseline values or with controls when present, without no adverse reaction related to the device. The authors concluded that there is a need for more and better designed RCTs, to confirm with a stronger level of evidence the promising preliminary results achieved by the current research.

Although originally cleared for marketing in 2008, the FDA rescinded the marketing clearance for Menaflex as it concluded that the device is intended to be used for different purposes and is technologically dissimilar from devices already on the market.

In April 2013, a Washington DC federal judge upheld FDA in the Menaflex case (Thompson, 2013) – the court noted that the FDA acted properly and within its statutory authority when it re-classified ReGen Biologics Menaflex knee repair device and rescinded the company’s 510(k). The company filed a lawsuit in 2011 charging that FDA’s decision to withdraw the device’s clearance was arbitrary and capricious. The Food and Drug Administration’s Center for Devices and Radiological Health (CDRH) cleared the device in 2008 over objections of some reviewers that it provided little or no benefit to patients. The new agency leadership brought in by the Obama administration reviewed the earlier decision and determined that the device should not have been cleared because FDA’s review was influenced by outside pressure, including congressional lobbying. Ivy Sports Medicine subsequently became the successor in interest to ReGen, according to the court.
Hirschmann et al (2013) evaluated the clinical and radiological outcomes after medial/lateral CMI at 12 months post-operatively. A total of 67 patients (47 males, mean age of 36 ± 10 years) underwent arthroscopic CMI after previous subtotal medial (n = 55) or lateral meniscectomy (n = 12) due to persistent joint line pain (n = 25) or to prophylactic reasons (n = 42). Clinical follow-up consisted of IKDC score, Tegner score, Lysholm score, and VAS for pain and satisfaction (pre-injury, pre-operatively, and 12 months post-operatively; follow-up rate 90 %); MRI scans were analyzed according to the Genovese criteria. A total of 19 patients (29 %) showed a normal (A), 35 nearly normal (B), 5 abnormal (C), and 1 patient severely abnormal total IKDC score (D). The median Tegner pre-injury score was 7 (range of 2 to 10) and at follow-up 6 (range of 2 to 10). The mean Lysholm score before surgery was 68 ± 20 and 93 ± 9 at follow-up. Pre-operatively, the mean VAS pain was 4.4 ± 3.1 and 2.0 ± 1.0 at follow-up. Clinical failure of the CMI occurred in 3 patients (n = 1 infection, n = 1 failure of the implant, n = 1 chronic synovitis). On MRI, the CMI was completely resorbed in 3 patients (5 %), partially resorbed in 55 (92 %), and entirely preserved in 3 (5 %) patients. In 5 patients (8 %) the CMI was iso-intense, in 54 (90 %) slightly and 1 (2 %) highly hyper-intense; 43 (72 %) patients showed an extrusion of the CMI implant of more than 3 mm. The authors concluded that significant pain relief and functional improvement throughout all scores at 1 year was noted. The CMI undergoes significant re-modeling, degradation, resorption, and extrusion in most of the patients. No difference in outcomes between the medial and lateral CMI was observed.

Bulgheroni et al (2014) compared the clinical, objective and radiographic long-term results of patients with anterior cruciate ligament (ACL) lesion and partial medial meniscus defects, treated with ACL reconstruction and partial medial meniscectomy or medial CMI implant. A total of 17 patients treated with combined ACL reconstruction and medial CMI and 17 patients treated with ACL reconstruction and partial medial meniscectomy were evaluated with mean follow-up 9.6 years with Lysholm, Tegner, objective and subjective International Knee Documentation Committee scores, and VAS for pain. Arthrometric evaluation was performed with KT 2000. Weight-bearing radiographs, antero-posterior and Rosenberg view, were also performed and evaluated with Kellgren-Lawrence score, Ahlback score and joint space narrowing. Pre-operative demographic parameters and clinical scores between patients treated with CMI and partial medial meniscectomy revealed no significant differences. A significant improvement of all the clinical scores was detected in both groups from pre-operative status to final follow-up. No significant difference between groups were found for clinical and radiographic scores; however, the chronic subgroup of patients treated with CMI showed a significantly lower level of post-operative knee pain compared to patients treated with partial medial meniscectomy and the acute subgroup of medial CMI showed better arthrometric scores. The authors concluded that good long-term clinical results in terms of stability, subjective outcomes and objective evaluation were reported both for medial CMI implant and partial medial meniscectomy, combined with ACL reconstruction for the treatment of partial medial meniscus tears combined with ACL lesions.
Chronic meniscal tears treated with medial CMI reported lower levels of post-operative pain compared to meniscectomy, while acute lesions treated with medial CMI showed less knee laxity. Therefore, the use of CMI in the case of anterior knee instability with a meniscal defect appears justified and able to improve clinical outcomes in the long-term. The findings of this small study need to be validated by well-designed studies.

Kaleka and colleagues (2014) stated that the preservation of meniscal tissue is paramount for long-term joint function, especially in younger patients who are athletically active. Many studies have reported encouraging results following the repair of meniscus tears, including both simple longitudinal tears located in the periphery and complex multi-planar tears that extend into the central third avascular region. However, most types of meniscal lesions are managed with a partial meniscectomy. Options to restore the meniscus range from an allograft transplantation to the use of synthetic and biological technologies. Recent studies have demonstrated good long-term outcomes with meniscal allograft transplantation, although the indications and techniques continue to evolve, and the long-term chondro-protective potential of this approach has yet to be determined. Several synthetic implants, most of which are approved in the European market, have shown some promise for replacing part of or the entire meniscus, including CMI, hydrogels, and polymer scaffolds. The authors concluded that currently, there is no ideal implant generated by means of tissue engineering. However, meniscus tissue engineering is a fast developing field that promises to develop an implant that mimics the histologic and biomechanical properties of a native meniscus.

Myers et al (2014) noted that there are 2 scaffold products designed for meniscal reconstruction or substitution of partial meniscal defects that are currently available in the Europe: (i) the collagen meniscal implant (CMI; Ivy Sports Medicine, Grafelfing, Germany) and the polymer scaffold (PS; Actifit, Orteq Bioengineering, London, United Kingdom). There are also several comparative studies that reported improved clinical scores in patients with chronic medial meniscus symptoms treated with CMI versus repeat partial meniscectomy, and a lower re-operation rate. Recently, PS insertion was shown to result in improved clinical outcomes in patients with chronic post-meniscectomy symptoms of the medial or lateral meniscus at short-term follow-up. However, the authors stated that there is currently no medium- or long-term data available for the PS. They stated that the use of meniscal scaffolds in the acute setting has not been found to result in improved outcomes in most studies.

In a multi-center study, Zaffagnini et al (2015) presented the 2-year results of the use of the lateral CMI for the treatment of irreparable lateral meniscal lesions or partial lateral meniscal defects, investigated the potential predictors of clinical results, and monitored device safety. A total of 43 patients with a mean age of 30.1 ± 12.0 years were clinically evaluated 24 months
after treatment of partial lateral meniscal defects with the CMI. These investigators used the Lysholm score, the Tegner Activity Scale, a VAS for pain (during strenuous activity, during routine activity, and at rest), a functional questionnaire, and a satisfaction questionnaire for the evaluation. All demographic and surgical parameters were used for multiple regression analysis to find outcome predictors. Serious adverse events and re-operations were monitored. All clinical scores significantly improved from pre-operatively to final evaluation at 24.2 ± 1.9 months’ follow-up. The Lysholm score improved significantly from 64.3 ± 18.4 pre-operatively to 93.2 ± 7.2 at final follow-up (p = 0.0001). Functional improvement was detected from 6 months after surgery, whereas strenuous activities and knee swelling reached optimal results after 12 months. The highest pain ratings experienced during strenuous activity, during routine activity, and at rest significantly improved from 59 ± 29, 29 ± 25, and 20 ± 25, respectively, pre-operatively to 14 ± 18, 3 ± 5, and 2 ± 6, respectively, at 2 years' follow-up (p = 0.0001). At final follow-up, 58 % of patients reported activity levels similar to their pre-injury values whereas 95 % of patients reported that they were satisfied with the procedure. A higher body mass index (BMI), the presence of concomitant procedures, and a chronic injury pattern seemed to negatively affect the final outcomes. Serious adverse events with a known or unknown relation to the scaffold, such as pain, swelling, and scaffold resorption, were reported in 6 % of patients, leading to CMI explantation, debridement, or synovectomy. The authors concluded that the lateral CMI scaffold could be considered a potentially safe and effective procedure to treat both irreparable lateral meniscal tears and post-meniscectomy syndrome in appropriately selected patients. Chronic injury, high BMI, and concomitant procedures have been shown to negatively affect the short-term results; however, the results appeared to slowly improve through the 24-month follow-up period. This case-series study provided Level IV evidence; its major drawbacks were small sample size (n = 430 and short-term follow-up (24 months).

Furthermore, an UpToDate review on “Meniscal injury of the knee” (Anderson, 2015) does not mention collagen meniscal implant/scaffold as a management tool.

Mutsaerts and associates (2016) compared the outcomes of various surgical treatments for meniscal injuries including (i) total and partial meniscectomy; (ii) meniscectomy and meniscal repair; (iii) meniscectomy and meniscal transplantation; (iv) open and arthroscopic meniscectomy; and (v) various different repair techniques. The Bone, Joint and Muscle Trauma Group Register, Cochrane Database, Medline, Embase and CINAHL were searched for all (quasi) RCTs comparing various surgical techniques for meniscal injuries. Primary outcomes of interest included patient-reported outcomes scores, return to pre-injury activity level, level of sports participation and persistence of pain using the VAS. Where possible, data were pooled and a meta-analysis was performed. A total of 9 studies were included, involving a combined 904 subjects, 330 patients underwent a meniscal repair, 402 meniscectomy and 160 a CMI. The...
only surgical treatments that were compared in homogeneous fashion across more than 1 study were the arrow and inside-out technique, which showed no difference for re-tear or complication rate. Strong evidence-based recommendations regarding the other surgical treatments that were compared could not be made. The authors concluded that the findings of this meta-analysis illustrated the lack of level I evidence to guide the surgical management of meniscal tears.

Bulgheroni and colleagues (2016) compared the effectiveness of 2 different meniscal scaffolds in treating patients with irreparable partial medial meniscal tear and patients complaining of pain in the medial compartment of the knee due to a previous partial medial meniscectomy. Based on previous studies, these researchers hypothesized that both the scaffolds are effective in improving clinical outcomes in these patient populations. A total of 28 patients underwent collagen-based medial meniscus implantation (CMI-Menaflex) and 25 with a second-generation scaffold (Actifit). All patients were assessed with Lysholm, Tegner scale, and MRI evaluation: pre-operatively, at 6 months, at 12 months, and followed-up for a minimum of 2 years. Second look arthroscopy and concomitant biopsy were performed in 7 and 12 patients of CMI and Actifit groups, respectively. The CMI group at final follow-up showed improvement in Lysholm score from 58.4 ± 17.3 to 94.5 ± 6.0, while the Actifit group showed improvement from 67.0 ± 15.7 to 90.3 ± 13.1; the improvement was statistically significant in both the groups, but inter-group difference was not statistically significant (p = 0.1061). Tegner Activity Scale score improved in both the groups, but inter-group difference was not statistically significant (p = 0.5918). MRI evaluation showed in-situ scaffold and no progression of degenerative arthritis in both the groups at final follow-up. Histological evaluation showed more fibrous tissue with blood vessels in the CMI group and the Actifit group showed avascular cartilaginous features. The authors concluded that both the scaffolds were effective in improving patients’ symptoms and joint function at short-term follow-up. The main drawbacks of this study were its small sample size (n = 28 for the Menaflex group) and short-term follow-up (2 years).

Lin and colleagues (2017) stated that meniscal injury is a common problem among sportsmen and increasingly seen in the older and more active population. The traditional treatment options include a partial meniscectomy, which provides good mechanical and pain relief to the patient. However, the focus of treatment is shifting towards repairing meniscal tears where possible and replacement of the lost meniscal tissue where appropriate. Replacement can be total or partial. Total meniscal replacement using an allograft, is usually reserved for young patients, who meet certain criteria and who have undergone several subtotal meniscectomies or a single-stage total meniscectomy and are still symptomatic. Partial meniscal replacement can be utilized in conjunction with a partial meniscectomy to fill the resulting space left by the resection. The authors noted that collagen-based implants and synthetic scaffolds have entered the European
market but have demonstrated mixed results in clinical trials. They stated that tissue engineering to create an implant that mimics the biomechanical properties holds much potential for future research.

Sun and colleagues (2017) stated that current surgical treatments for meniscal tears suffer from subsequent degeneration of knee joints, limited donor organs and inconsistent post-treatment results. Three clinical scaffolds (Menaflex CMI, Actifit scaffold and NUsurface Meniscus Implant) are available on the market. Menaflex CMI and Actifit scaffold are partial meniscal substitutes with equivalents in histological, radiological, and clinical evaluations. They have received the Conformite Europeenne (CE) mark in Europe, whereas the FDA believes that additional data are needed to confirm their efficacy on chondral degradation and prevention of osteoarthritis development. Thus, many scaffold-based research activities have been carried out to develop new materials, structures and fabrication technologies to mimic native meniscus for cell attachment and subsequent tissue development, and restore functionalities of injured meniscus for long-term effects. This review began with a synopsis of relevant structural features of meniscus and went on to describe the critical considerations. Promising advances made in the field of meniscal scaffolding technology, in terms of biocompatible materials, fabrication methods, structure design and their impact on mechanical and biological properties were discussed in detail. Among all the scaffolding technologies, additive manufacturing (AM) is very promising because of its ability to precisely control fiber diameter, orientation, and pore network micro-architecture to mimic the native meniscus micro-environment.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+".

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<tr>
<td>G0428</td>
<td>Collagen meniscus implant procedure for filling meniscal defects (e.g., CMI, Collagen Scaffold, Menaflex)</td>
</tr>
<tr>
<td></td>
<td>ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):</td>
</tr>
<tr>
<td>M17.0 - M17.9</td>
<td>Osteoarthritis of knee</td>
</tr>
<tr>
<td>M22.2x1 - M23.92</td>
<td>Internal derangement of knee</td>
</tr>
<tr>
<td>Q68.6</td>
<td></td>
</tr>
<tr>
<td>M25.161 - M25.169</td>
<td>Other specified disorders of knee joint</td>
</tr>
<tr>
<td>M25.861 - M25.869</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>M25.261 - M25.269</td>
<td>Other joint derangement of knee</td>
</tr>
<tr>
<td>M25.361 - M25.369</td>
<td>Pain in knee</td>
</tr>
<tr>
<td>M93.261 - M93.269</td>
<td>Osteochondritis dissecans knee</td>
</tr>
<tr>
<td>S83.211+ - S83.249+</td>
<td>Tear of medial cartilage or meniscus of knee, current injury</td>
</tr>
<tr>
<td>S89.90x+ - S89.92x+</td>
<td>Injury of knee</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


17. U.S. Food and Drug Administration. FDA determines knee device should not have been cleared for marketing. Decision follows re-evaluation of scientific evidence. FDA News Release. Silver Spring, MD: FDA; October 14, 2010.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0786
Menaflex

There are no amendments for Medicaid.