7.01.160	Synthetic Cartilage Implants for Joint Pain		
Original Policy Date:	February 1, 2018	**Effective Date:**	November 1, 2023
Section:	7.0 Surgery	**Page:**	Page 1 of 15

Policy Statement

I. Synthetic cartilage implants are considered **investigational** for the treatment of articular cartilage damage.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

The following codes are specific to this procedure:

- **28291**: Hallux rigidus correction with cheilectomy, debridement and capsular release of the first metatarsophalangeal joint; with implant

There is no specific code to the Cartiva "Hydrogel" Implant. The following HCPCS code may be billed:

- **L8699:** Prosthetic Implant, not otherwise specified

The following codes may be found on claims since the codes describe various materials such as silicone or titanium:

- **L8641:** Metatarsal join
- **L8642:** Hallux implant

Description

Articular cartilage damage, either from a focal lesion or diffuse osteoarthritis (OA), can result in disabling pain. Cartilage is a hydrogel, comprised mostly of water with collagen and glycosamino-glycans, that does not typically heal on its own. There is a need for improved treatment options. In 2016, a synthetic polyvinyl alcohol hydrogel disc received marketing approval by the U.S. Food and Drug Administration for the treatment of degenerative or posttraumatic arthritis in the first metatarsophalangeal (MTP) joint. If proven successful for the treatment of the MTP joint, off-label use is likely.

Related Policies

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

Benefit Application

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

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

Regulatory Status

The Cartiva PVA implant was approved by the U.S. Food and Drug Administration (FDA) in 2016 for the treatment of arthritis of the MTP joint. It has been distributed commercially since 2002 with approval in Europe, Canada, and Brazil. The Cartiva Synthetic Cartilage Implant (Wright Medical, Alpharetta, GA) was approved by the FDA through the premarket approval process (P150017) for painful degenerative or posttraumatic arthritis in the first MTP joint along with hallux valgus or hallux limitus and hallux rigidus. Lesions greater than 10 mm in size and insufficient quality or quantity of bone are contraindications. Continued approval depends on a study evaluating long-term safety and effectiveness. The post-approval study will follow the subjects treated with Cartiva Synthetic Cartilage Implant for 5 years. FDA product code: PNW.

Rationale

Background

Articular Cartilage Damage

Articular cartilage damage may present as focal lesions or as more diffuse osteoarthritis. Cartilage is a biological hydrogel that is comprised mostly of water with collagen and glycosaminoglycans and does not typically heal on its own. Osteoarthritis or focal articular cartilage lesions can be associated with substantial pain, loss of function, and disability. Osteoarthritis is most frequently observed in the knees, hips, interphalangeal joints, first carpometacarpal joints, first metatarsophalangeal (MTP) joint, and apophyseal (facet) joints of the lower cervical and lower lumbar spine. Osteoarthritis less commonly affects the elbow, wrist, shoulder, and ankle. Knee osteoarthritis is the most common cause of lower-limb disability in adults over age 50, however, osteoarthritis of the MTP joint with loss of motion (hallux rigidus) can also be severely disabling due to pain in the "toe-off" position of gait. An epidemiologic study found that osteoarthritis of the first MTP joint may be present in as many as 1 in 40 people over the age of 50.[1,]

Treatment

Treatment may include debridement, abrasion techniques, osteochondral autografting, and autologous chondrocyte implantation. Debridement involves the removal of the synovial membrane, osteophytes, loose articular debris, and diseased cartilage and is capable of producing symptomatic relief. Subchondral abrasion techniques attempt to restore the articular surface by inducing the growth of fibrocartilage into the chondral defect. Diffuse osteoarthritis of the knee, hip, shoulder or ankle may be treated with joint replacement.

Early-stage osteoarthritis of the first MTP joint is typically treated with conservative management, including pain medication and change in footwear. Failure of conservative management in patients with advanced osteoarthritis of the MTP joint may be treated surgically. Cheliectomy (removal of bone osteophytes) and interpositional spacers with autograft or allograft have been used as temporary measures to relieve pain.

Although partial or total joint replacement have been explored for MTP osteoarthritis, complications from bone loss, loosening, wear debris, implant fragmentation, and transfer metatarsalgia are not uncommon. Also, since the conversion of a failed joint replacement to arthrodesis has greater complications and worse functional results than a primary arthrodesis (joint fusion), MTP arthrodesis is considered the most reliable and primary surgical option. Arthrodesis can lead to a pain-free foot, but the loss of mobility in the MTP joint alters gait, may restrict participation in running and other sports, and limits footwear options, leading to patient dissatisfaction. Transfer of stress and arthritis in an adjacent joint may also develop over time.

Because of the limitations of MTP arthrodesis, alternative treatments that preserve joint motion are being explored. Synthetic cartilage implants have been investigated as a means to reduce pain and

improve function in patients with hallux rigidus. Some materials such as silastic were found to fragment with use. Other causes of poor performance are the same as those observed with metal and ceramic joint replacement materials and include dislocation, particle wear, osteolysis, and loosening.

Synthetic polyvinyl alcohol (PVA) hydrogels have water content and biomechanical properties similar to cartilage and they are biocompatible. Polyvinyl alcohol hydrogels have been used in a variety of medical products including soft contact lens, artificial tears, hydrophilic nerve guides, and tissue adhesion barriers. This material is being evaluated for cartilage replacement due to the rubber elastic properties and, depending on the manufacturing process, high tensile strength and compressibility.[2,]

The Cartiva implant is an 8- to 10 mm PVA disc that is implanted with a slight protrusion to act as a spacer for the first MTP joint. It comes with dedicated reusable instrumentation, which includes a drill bit, introducer, and placer.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the 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 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 technology, 2 domains are examined: the relevance, and 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. Randomized controlled trials 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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Early-Stage First Metatarsophalangeal Osteoarthritis

Clinical Context and Therapy Purpose

The purpose of a synthetic cartilage implant in individuals who have early-stage first metatarsophalangeal (MTP) joint osteoarthritis (OA) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with early-stage first MTP OA.

Interventions
The therapy being considered is the Cartiva synthetic cartilage implant.

Comparators
The following therapies are currently being used:

- Conservative nonoperative treatment which would include modification of footwear and non-steroidal anti-inflammatory drugs (NSAIDS).
- Cheilectomy

Outcomes
The general outcomes of interest are symptoms, typically measured with a visual analog score (VAS) for pain. Functional outcomes and quality of life are measured with the Foot and Ankle Ability Measure (FAAM). The FAAM is a validated measure of sports activities and activities of daily living (ADL), with a minimal clinically important difference defined as 9 points for sports and 8 points for ADL subscales. Adverse events from the implantation procedure would be measured within 30 days, while dislocation and wear would be monitored at 5 to 10 years.

A beneficial outcome of the implant would be a reduction in pain and improvement in function.
A harmful outcome of the implant would be an increase in pain and a reduction in function.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
No studies were identified on the use of synthetic cartilage implants for early-stage first MTP OA.

Section Summary: Early-Stage First Metatarsophalangeal Osteoarthritis
The evidence is insufficient to determine the effects of the synthetic cartilage implant for early-stage first MTP OA. RCTs and long-term follow-up are needed to determine implant survival and its effect on health outcomes.

Advanced First Metatarsophalangeal Osteoarthritis
Clinical Context and Therapy Purpose
The purpose of a synthetic cartilage implant in individuals who have advanced first MTP OA is to provide a treatment option that is an alternative to or an improvement on existing therapies.
The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with advanced MTP OA.

Interventions
The therapy being considered is the Cartiva synthetic cartilage implant.

Comparators
The following therapies are currently being used:

- Conservative nonoperative treatment which would include modification of footwear and NSAIDS.
- Cheilectomy
- Arthrodesis

Outcomes

The general outcomes of interest are symptoms, typically measured with a VAS for pain. Functional outcomes and quality of life are assessed with the FAAM. Adverse events from the implantation procedure would be measured within 30 days while harms from dislocation and wear would be measured at 5 to 10 years.

A beneficial outcome of the implant would be a reduction in pain and improvement in function.
A harmful outcome of the implant would be an increase in pain and a reduction in function.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Review

Smyth et al (2020) conducted a systematic review of PVA implants in patients with hallux rigidus. The authors identified 7 publications, 6 of which were related to the key randomized controlled trial described below, and the final publication was a case series by Cassenelli et al (2019) which is also included below.[3,4,5,] The systematic review noted the lack of information independent of the original RCT as a primary limitation.[4,] They concluded that a moderate recommendation can be given for use of a polyvinyl alcohol implant in the short-term, but long-term data are lacking.

Randomized Controlled Trial

The U.S. Food and Drug Administration (FDA) approval of the Cartiva synthetic cartilage implant was based on an unmasked, multicenter, noninferiority trial (Cartiva MOTION) that compared the implant with arthrodesis of the first MTP joint (see Table 1). This study was published by Baumhauer et al (2016).[6,3,] The primary outcome was a composite of a 30% or greater difference in VAS scores for pain, maintenance of function on the FAAM ADL subscale, and absence of major safety events at 2 years. The primary effectiveness endpoint was achieved by 80% of patients in both groups, and the implant met the 15% noninferiority margin (p<.0075).

Table 1. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Active Intervention	Comparator Intervention
Baumhauer et al (2016);[3,] MOTION	US, Canada, EU	12	2009-2012	197 patients with advanced hallux rigidus (Coughlin grade 2, 3, or 4 [see Appendix Table 1]) with VAS $\geq$ 40/100. Patients were excluded if they had lesions > 10 mm in size, hallux varus to any degree, or hallux valgus > 20	132 patients received the Cartiva cartilage implant	65 patients underwent arthrodesis

RCT: Randomized controlled trial; VAS: visual analog score

VAS pain scores decreased significantly in both groups but were consistently lower in the arthrodesis group from 6 weeks through 2 years (see Table 2). Nearly all patients (97%) who underwent fusion had 30% or greater relief in pain compared with 89% of patients who received the implant.

Maintenance of function, as measured by the FAAM ADL subscale, was observed in 98.3% of patients who received the implant and in 97.6% of patients who underwent fusion. Fourteen (9.2%) implants were removed and converted to arthrodesis, while in the arthrodesis group 6 (12%) patients had removal of screws or screws and plates. As expected, dorsiflexion was significantly better in the implant group (29) than in the fusion group (15; p<.001). Radiographic measurements showed 4 (8%) occurrences of mal-union or non-union in the fusion group and no device displacement, fragmentation, or avascular necrosis with the implant. Some instances of radiolucency, bony reactions, and heterotopic ossification were observed, but these events did not correlate with individual patient success.

Glazebrook et al (2018) reported a reduction in operative and recovery time with the implant compared to arthrodesis.[7,] Additional analysis of data (2017) from the pivotal trial did not identify any factors (e.g., hallux rigidus grade, preoperative pain, duration of symptoms, body mass index) that affected the success of the procedure.[8,] The analysis raised questions whether Coughlin grade (symptoms, radiographic measures, range of motion), is the most appropriate method to identify patients for the procedure, leading the investigators to recommend using only clinical signs and symptoms to guide treatment.[9,]

Table 2. Outcome Scores for Synthetic Cartilage Implant and Arthrodesis

Outcomes	Baseline	6 Weeks	3 Months	6 Months	1 Year	2 Years
VAS pain						
Implant	68 (13.9)	33.3 (24.7)	29.4 (23.2)	28.9 (27.75)	17.8 (23.0)	14.5 (22.1)
Arthrodesis	69.3 (14.3)	17.2 (17.6)	15.5 (13.1)	11.7 (18.3)	5.7 (8.5)	5.9 (12.1)
p-value	.571	<.001	<.001	<.001	.001	.002
FAAM ADL						
Implant	59.4 (16.9)	69.0 (19.0)	77.3 (17.70)	82.7 (17.5)	88.6 (14.4)	90.4 (15.0)
Arthrodesis	56.0 (16.8)	59.6 (24.8)	82.5 (14.9)	89.9 (12.4)	94.1 (6.8)	94.6 (7.1)
p-value	.222	.008	.079	.014	.018	.082
FAAM sports						
Implant	36.9 (20.9)	39.5 (26.3)	55.1 (26.5)	66.6 (26.3)	75.8 (24.8)	79.5 (24.6)
Arthrodesis	35.6 (20.5)	22.4 (22.5)	53.9 (29.5)	78.6 (23.8)	84.1 (16.9)	82.7 (20.5)
p-value	.694	<.001	.804	.010	.043	.461

Values are mean (standard deviation).
ADL: activities of daily living; FAAM: Foot and Ankle Ability Measure; VAS: visual analog score.
A selection of results from the FAAM ADL questionnaire, which is made up of 21 related questions, were reported on the FDA's Summary of Safety and Effectiveness (see Table 3).[6,] Only the "Up on Toes" was superior in the Cartiva group. Of concern is the greater difficulty of the Cartiva group (Moderate Difficulty, Extreme Difficulty, and Unable to Do) compared to the arthrodesis group for walking for 15 min (16% vs. 0%), Up Stairs (6% vs. 0%) and Squats (19% vs. 8%).

Table 3. Foot and Ankle Ability Measure (FAAM) Activities of Daily Living Questionnaire Excerpt

Outcomes	Group	No Difficulty	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to Do
Daily Activities	Arthrodesis	94%	6%	0%	0%	0%
	Cartiva	88%	10%	0%	2%	0%
Walk 15 Min	Arthrodesis	85%	13%	0%	0%	0%
	Cartiva	67%	17%	9%	5%	2%
Upstairs	Arthrodesis	87%	13%	0%	0%	0%
	Cartiva	83%	10%	4%	2%	0%
Up on Toes	Arthrodesis	36%	28%	17%	9%	11%
	Cartiva	37%	33%	15%	7%	9%
Squat	Arthrodesis	70%	21%	6%	2%	0%
	Cartiva	57%	18%	11%	6%	2%

Limitations in relevance and design and conduct are shown in Tables 4 and 5.

Table 4. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Baumhauer et al (2016);[3,] MOTION				**2. Range of motion is an intermediate measure.**	**1,2. Follow-up in this publication was for 2 years, but the Cartiva group will be followed for 5 years.**

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 5. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Baumhauer et al (2016);[3,] MOTION				1. Withdrawals after randomization were higher in the control group (15/65 vs. 2/132), suggesting possible bias in expectations and subjective outcome assessments in favor of the novel joint preserving procedure. A modified intention-to-treat analysis was requested by the U.S. Food and Drug Administration to adjust for the difference in study withdrawals. The modified intention-to-treat analysis included 130 patients in the Cartiva group and 50 patients in the fusion group.		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

An FDA regulated safety and efficacy follow-up study was required through 5 years.[10,11,] The patients in the follow-up study included the randomized and nonrandomized run-in group who received the implant for a total of 152 patients (see Table 6) but did not include the arthrodesis group. By year 5,

15.1% of the implant group had undergone removal and conversion to arthrodesis (see Table 7). The overall Kaplan-Meier synthetic cartilage implant survivorship at 5.8 years of follow-up was 84.9%. Of the patients who retained the implant, 97.2% reported a clinically significant improvement in pain, 90.5% reported a clinically significant improvement in FAAM ADL, and 93.3% reported a clinically significant improvement in FAAM sports. Independent radiographic review found no evidence of avascular necrosis, device migration, or fragmentation. Because there was no follow-up of the arthrodesis arm from the randomized trial, conclusions about the comparative effectiveness of the 2 treatment options are limited.

Comparative Observational Study

Joo et al (2021) conducted a retrospective review of 181 patients who underwent arthrodesis (n=122) or Cartiva implant (n=59) at their institution.[12,] At baseline, patients receiving Cartiva had higher physical function scores (47.1) than those undergoing arthrodesis (43.9: p<.01), and this difference remained significant at the mean final follow up of 33 months (51.4 vs. 45.9; p<.01). Pain interference scores were similar between groups at baseline (57.4 vs. 55.6; p=.07) and remained similar at final follow up (46.9 vs. 48.2; p=.49). Significant pain was reported by 4 patients (10%) in the Cartiva group and 5 patients (8%) in the arthrodesis group at final follow-up (p=.76). Complications occurred in 3 (2.4%) patients in the arthrodesis group and 2 (3%) in the Cartiva group (p=.72).

Case Series

Cassinelli et al (2019) conducted a retrospective review of early outcomes and complications from the Cartiva implant for the treatment of hallux rigidus at their institution.[5,] Sixty consecutive patients treated between August 2016 and April 2018 with a mean of 15 months of follow-up (range, 2 to 30) were included. Out of 60 patients (64 implants), 30% of patients underwent magnetic resonance imaging (MRI) due to pain, 20% had additional surgery and 38% were unsatisfied or very unsatisfied. Magnetic resonance imaging showed residual capsular inflammation, bone marrow edema, and degenerative changes/edema of the phalanx or metatarsal. A limitation of these results is that 45% of patients underwent additional procedures at the time of implantation and 23% had prior surgery of the hallux. Therefore, these results are not representative of isolated implant procedures, but may be indicative of results outside of the investigational setting.

In a subsequent report, An et al (2019) provided further detail on the 16 of 60 (27%) treated patients from their institution who were evaluated for persistent pain following Cartiva implantation.[13,] There was a reduction of joint space on plain radiographs, MRI showed a reduction in implant diameter from 10 mm to 9.7 (standard deviation [SD] 0.4) mm and bony channel widening to 11.2 (SD 0.8) mm. Peri-implant fluid suggested instability at the implant-bone interface. There was also evidence of subsidence, with the implant below the subchondral bone of the metatarsal head, and persistent edema was observed in all 16 cases. Radiographic findings from another series of 27 consecutive patients by Shi et al (2019) also suggested subsidence of the implant into the soft medullary canal.[14,] An analysis of the Manufacturer and User Facility Device Experience (MAUDE) also found subsidence to be a concern with 16 voluntary reports between July 2016 and October 2019.[15,] It has been noted that the implants in the reports by Cassinelli et al and An et al were initially seated 2 to 2.5 mm above the adjacent bone, rather than the 0.5 to 1.5 mm that is recommended by the manufacturer.[16,17,] Further study is needed to clarify these issues.

Table 6. Summary of Key Case Series Characteristics

Study	Country/institution	Participants	Follow-Up
Glazebrook et al (2018)[11,]	US, Canada, EU	152 randomized and roll-in patients treated with Cartiva cartilage implant from the pivotal trial	5 yr
Cassinelli et al (2019)[5,]	US	60 patients who received the Cartiva implant between August 2016 and April 2018	

Table 7. Summary of Key Case Series Results

Study	Baseline	Follow-up	
Glazebrook et al (2018)[11,]		2 Year	5 Year
n (%)	152	135 (88.8%)	112 (73.6%)
Cumulative Device Removals, n (%)		14/135 (10.4%)	23/112 (20.5%)
Number of Patients with Device Present at 5 Years and Assessed for Clinical Outcomes	106	106	106
Patients Reporting Pain VAS ≥30% decrease		100/106 (94.3%)	103/106 (97.2%)
FAAM ADL ≥8 points increase, n (%)		98/105 (93.3%)	95/105 (90.5%)
FAAM Sports ≥9 points increase		94/103 (91.3%)	97/104 (93.3%)
Cassinelli et al (2019)[5,]		15 mo (range 2 - 30)	
Patients unsatisfied and very unsatisfied	64	24/64 (38%)	
Magnetic resonance imaging due to pain		19/64 (30%)	
Reoperation Rate		13/64 (20%)	

ADL: activities of daily living; FAAM: Foot and Ankle Ability Measure; VAS: visual analog score.

Section Summary: Advanced First Metatarsophalangeal Osteoarthritis

Results at 2 years from the pivotal non-inferiority trial showed pain scores that were slightly worse compared to patients treated with arthrodesis and similar outcomes between the groups for ADL and sports. In a non-inferiority trial, some benefit should be observed to justify the non-inferiority margin. However, the benefit of Cartiva with respect to increased range of motion does not appear to translate to improved ADL, sports activities, or patient report of well-being compared to arthrodesis. In addition, the Cartiva group showed a higher rate of adverse outcomes (Moderate Difficulty, Extreme Difficulty, and Unable to Do) compared to the arthrodesis group for walking for 15 min (16% vs. 0%), Up Stairs (6% vs. 0%) and Squats (19% vs. 8%). Some bias in favor of the novel motion preserving implant was also possible, as suggested by the high dropout rate in the arthrodesis group after randomization. Five-year follow-up of both the randomized and run-in patients who received an implant was reported in 2018 for 135 of 152 patients. At this time point, 15% of implants had been removed with conversion to arthrodesis. There are additional safety signals in an independent study by Cassinelli et al (2019) and An et al (2019). In that report, 30% of patients underwent magnetic resonance imaging due to pain, 20% had additional surgery and 38% were unsatisfied or very unsatisfied. A retrospective comparative observational study found few differences in either safety or efficacy between arthrodesis and Cartiva with a limited mean follow-up of 33 months. Further long-term study of potential adverse events with this novel technology is needed. In addition, comparison to arthrodesis at long-term follow-up is needed to determine whether the implant improves function. Corroboration of long-term results in an independent RCT is also needed to determine the effect of the implant on health outcomes.

Articular Cartilage Damage of Joints Other Than the Great Toe

Clinical Context and Therapy Purpose

The purpose of a synthetic cartilage implant in individuals who have advanced OA of joints other than the first MTP joint is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with OA of joints other than the MTP joint.

Interventions
The therapy being considered is the synthetic cartilage implant.

Comparators
The following therapies are currently being used:

- Conservative nonoperative treatment
- Osteochondral autografting
- Autologous chondrocyte implantation
- Arthroplasty

Outcomes
The general outcomes of interest are symptoms, typically measured with a VAS for pain. Functional outcomes and quality of life are measured with questionnaires such as the FAAM. Adverse events from the implantation procedure would be measured within 30 days while harms from dislocation and wear would be measured at 5 to 10 years.

A beneficial outcome of the implant would be a reduction in pain and improvement in function.
A harmful outcome of the implant would be an increase in pain and a reduction in function.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Use of polyvinyl alcohol hydrogel implants has been reported in a few observational studies for articular cartilage lesions of the knee and the second MTP joint. A study is in progress to evaluate the polyvinyl alcohol hydrogel implant for OA of the first carpometacarpal joint, but the study is not expected to be completed until 2024 (see Table 8). No other RCTs on synthetic cartilage implants for joints other than the great toe have been identified.

Section Summary: Articular Cartilage Lesions of Joints Other Than the Great Toe
The evidence is insufficient to determine the effects of the synthetic cartilage implant for joints other than the great toe. Randomized controlled trials and long-term follow-up are needed to determine implant survival and the effect on health outcomes.

Supplemental Information
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest. No guidelines or statements were identified.

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

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 8.

Table 8. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03247439[a]	A Prospective Study to Evaluate the Safety and Effectiveness of the Cartiva® Synthetic Cartilage Implant for CMC in the Treatment of First Carpometacarpal Joint Osteoarthritis as Compared to Ligament Reconstruction Tendon Interposition (LRTI) Comparator (GRIP2)	74	Mar 2024
Unpublished			
NCT02391506[a]	A Prospective Study to Evaluate the Safety and Effectiveness of the Cartiva® Synthetic Cartilage Implant for CMC in the Treatment of First Carpometacarpal Joint Osteoarthritis	50	Mar 2019
NCT03935880	Treatment of Hallux Rigidus With Synthetic Hemiarthroplasty Versus Cheilectomy: A Randomized Controlled Trial	20 (actual)	Sep 2021 (terminated due to difficulty meeting recruitment goals)

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

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Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	28291	Hallux rigidus correction with cheilectomy, debridement and capsular release of the first metatarsophalangeal joint; with implant
HCPCS	L8641	Metatarsal joint implant

Type	Code	Description
	L8642	Hallux implant
	L8699	Prosthetic implant, not otherwise specified

Policy History

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

Effective Date	Action
02/01/2018	BCBSA Medical Policy Adoption
05/01/2019	Policy revision without position change
09/01/2019	Policy revision without position change
09/01/2020	Annual review. No change to policy statement. Literature review updated.
09/01/2021	Annual review. No change to policy statement. Literature review updated.
09/01/2022	Annual review. No change to policy statement. Literature review updated.
11/01/2023	Annual review. No change to policy statement. Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

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

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

Prior Authorization Requirements and Feedback (as applicable to your plan)

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

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

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

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Synthetic Cartilage Implants for Joint Pain 7.01.160 **Policy Statement:** I. Synthetic cartilage implants are considered **investigational** for the treatment of articular cartilage damage.	**Synthetic Cartilage Implants for Joint Pain 7.01.160** **Policy Statement:** I. Synthetic cartilage implants are considered **investigational** for the treatment of articular cartilage damage.