Molina Clinical Policy
Genicular Artery Embolization of the Knee for Osteoarthritis
Policy No. 410

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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Osteoarthritis (OA), also referred to as degenerative joint disease, is the most common form of arthritis worldwide and a leading cause of disability among older adults (United States Bone and Joint Initiative, 4th ed.). OA of the knee is the result of cumulative stress and degeneration of the articular cartilage. As the cartilage wears down, there is a loss of joint space with increased shear forces and stress on the capsule. The synovial membrane becomes irritated and inflamed, with thickening and knee effusion resulting in a swollen and painful joint. Currently, there is no cure for OA. Existing treatments aim to reduce pain and alleviate symptoms, as well as improve and preserve range of motion, function, and health-related quality of life. Treatment options for knee OA are available depending on disease severity and commonly include a combination of nonpharmacologic and pharmacologic therapies. Nonpharmacologic interventions include weight management, exercises, physical therapy, and assistive devices (i.e., canes, walkers, braces, and foot orthoses). Pharmacologic therapies include acetaminophen, topical capsaicin, oral and topical nonsteroidal anti-inflammatory drugs (NSAIDs), duloxetine, and intraarticular glucocorticoids. Surgical treatment, such as partial or total knee replacement, is reserved for severe joint disease, pain, and functional limitations refractory to both pharmacological and nonpharmacological treatment modalities (OARSI, 2019).

Geniculate artery embolization (GAE) is an interventional radiology procedure used to treat knee pain due to OA by reducing blood flow to the lining of the knee, or the synovium, as pain in knee OA is often caused by increased blood flow to the knee related to inflammation. The inflammatory component in the pathogenesis is thought to be associated with increased angiogenesis; therefore, small vessels can be temporarily or permanently obliterated by interventional radiology embolization (Torkian et al., 2021). GAE is an outpatient procedure that uses moderate sedation. During the procedure, a vascular interventionalist inserts a small catheter into the femoral artery in the groin and guides it using moving X-ray imaging to the arteries carrying blood to the lining of the knee (Padia et al., 2021). Tiny beads are injected into these arteries via catheter to embolize, block, and reduce blood supply to the area of inflammation. Images of the patient's leg can be examined in real time during image-guided surgery. Patients may experience temporary increased knee pain following the procedure, however the pain may be alleviated or eradicated over the course of several weeks. GAE provides another minimally invasive, nonsurgical intervention treatment option for patients with symptomatic knee OA who are unwilling or unable to undergo surgery.

Regulatory Status

Embolic agents applied in GAE for OA were classified as temporary and permanent embolic agents and included (but were not limited to) Embozene, imipenem/cilastatin, resorbable microspheres, and polyvinyl alcohol.

- Embozene consists of spherical, biocompatible, nonresorbable, polymer-coated hydrogel particles that are available in a range of sizes. The FDA granted Breakthrough Device Designation for Embozene microspheres for GAE for symptomatic knee OA. Embozene is currently FDA-cleared for the embolization of hypervascular tumors, arteriovenous malformations, uterine fibroids, and benign prostatic hyperplasia (BPH).
- Embosphere (ES) Microspheres, a permanent embolization bead technology, are indicated for use in embolization of arteriovenous malformations, hyper vascular tumors, symptomatic uterine fibroids, and the prostate arteries for relief of symptoms related to BPH.

  - One study on the use of ES for GAE to treat mild-to-moderate knee OA has been published. In a prospective study, a total of 10 patients (15 knees) who had GAE underwent embolization with 100-to 300-µm ES particles. They were compared with a subsequent cohort of 11 patients (18 knees) who underwent GAE with imipenem-cilastatin (Jalaeian et al. 2021). Clinical outcomes were evaluated at 6-month and 24-month follow-up and compared to baseline using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire. At two-years follow-up, the researchers report clinical success in 61.5% of knees treated with the ES microspheres, versus a 53.8% clinical success rate in the Imipenum Cilastatin group. Both embolic materials resulted in a significant decrease in pain WOMAC and total WOMAC scores at six months compared to baseline, and the effect of GAE on pain WOMAC and total WOMAC scores was sustained until the 24-month follow-up visit in both groups.
  - Currently under investigation for GAE in 2 clinical trials: 1) NCT04662840: A three-arm prospective double-blinded randomized comparative trial comparing results of knee OA pain improvement in patients awaiting total knee arthroplasty by either a sham procedure, a GAE procedure or a geniculate nerve ablation procedure; 2) NCT05112926: A prospective, single arm investigation to evaluate the effectiveness and safety of ES Microspheres for embolization of the geniculate artery for the treatment of moderate to severe knee OA.
- Embosure Microspheres are resorbable, temporary, and do not permanently remain in the treated vessels. The FDA granted Breakthrough Device Designation for Embosure Microspheres to treat pain associated with knee OA in May 2021. As of December 1, 2021, no clinical trials had been registered.
- Optisphere/Gel-Bead (Teleflex), an absorbable gel-bead technology, is being evaluated for GAE for moderate-to-severe knee OA in NCT04951479. Gel-Beads are currently FDA-cleared for other embolization indications. Bagla et al. (2021) published a single-blinded, randomized controlled trial (RCT) comparing knee OA symptom reduction after GAE versus a sham procedure, which included 21 participants with mild to moderate OA and intractable knee pain who were randomized 2:1 to either GAE or a sham procedure. The study concluded that GAE results in greater symptomatic improvement than the sham procedure, with a clinically significant reduction in pain and disability in patients with mild to moderate knee OA.

COVERAGE POLICY

Genicular artery embolization for the treatment of osteoarthritis-related knee pain **is considered experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature that has not established long-term safety, efficacy, and effect on net health outcomes.

SUMMARY OF MEDICAL EVIDENCE

The best available published evidence evaluating Embozene Microspheres for GAE to treat symptomatic knee OA includes a prospective open-label study (Padia et al., 2021; NCT03491397) and a pilot study (Bagla et al., 2020; NCT02850068).

Padia et al. (2021) evaluated the safety and efficacy of GAE for the treatment of symptomatic knee OA in 40 patients aged 40 to 80 years (median age 69) with moderate or severe knee OA (based on the Kellgren-Lawrence score grade 2, 3, or 4) who had previously failed conservative therapies and were ineligible for or declined surgery in a prospective open-label study. Knee OA severity was grade 2 in 18% of patients, grade 3 in 43%, and grade 4 in 40%. Embolization of the knee was conducted with 100-µm particles (Embozene; Varian Medical Systems) and technical success was reported in 100% of the participants with a median procedure time of 79 minutes. The baseline severity of knee pain was assessed by a visual analog scale (VAS) score (range from 0 to 10) and the baseline symptoms related to knee OA were quantified using the WOMAC. The primary efficacy endpoint was the change in WOMAC score from baseline to 12 months after GAE with clinical success was defined as a 50% reduction in WOMAC score. The WOMAC total decreased by 61% and the VAS pain scores decreased by 67% at 12 months. A reduction of ≥ 50% in both WOMAC total and VAS pain scores was reported in 68% of patients (27 patients), while 43% patients were reported to experience a ≥ 75% reduction at 12 months. The median WOMAC score decreased from 52 to 19 at 12 months. Of 13 (33%) patients with < 50% improvement in the WOMAC score, 5 patients subsequently underwent total knee arthroplasty. The authors noted that the adverse events occurring at the knee included focal epidermal layer skin

ulceration in 7 patients (18%) occurring 7 to 10 days after GAE and resolving within 3 days; 2 cases of clinically asymptomatic bone infarct in the tibia and patella; and 1 case of focal fat necrosis of the lower thigh.

Bagla et al. (2020) conducted a pilot study of 20 patients to evaluate the efficacy and safety of embolization of hyperemic synovial tissue for the treatment of knee pain secondary to OA. The participants (mean age 59.4 years; (range 49-84 years) had radiographic knee OA and moderate-to-severe pain refractory to conservative therapy for at least 3 months. All patients underwent MRI before GAE and at 1 month after GAE. OA symptoms were assessed using WOMAC scores, and pain was assessed using VAS score (0 to 100 mm). Adverse events were recorded at all time points. GAE was performed with 75- or 100-µm micrometer Embozene Microspheres. The primary endpoint of clinical success was defined as a 20% change in VAS or 16% change in WOMAC score at 6 months without an increase in pain medication use or intra-articular injection. Embolization of at least 1 genicular artery was achieved in 20 of 20 (100%) patients. The mean GAE procedure time was 81 minutes. The decreases in VAS and WOMAC scores from baseline to 6 months were significant (VAS scores decreased from a mean of 76 mm at baseline to 22 mm at 1 month, 34 mm at 3 months, and 21 mm at 6 months; WOMAC scores decreased from 61 at baseline to 24 at 1 month, 31 at 3 months, and 31 at 6 months). No patients increased their pain medications from baseline during the study; 65% of patients reported a decrease in daily analgesic medication use. At 6 months, 80% of patients met the primary WOMAC endpoint, and 85% of patients met the primary VAS endpoint. Adverse events included skin discoloration at the knee in 13 cases that resolved within 3 months, and great toe plantar numbness in 2 patients that resolved within 2 weeks. The authors concluded that GAE to treat knee pain secondary to OA can be performed safely and demonstrates potential efficacy. However, further randomized comparative studies are needed to determine the true treatment effect versus the placebo effect.

Systematic Analysis/Meta-Analyses

Two meta-analyses on GAE evaluated knee OA and included data on Embozene (Torkian et al., 2021; Casabadan et al., 2021).

This meta-analysis includes 11 studies that reported on 268 knees in 225 patients who were treated for GAE with various embolic agents; 72 patients were administered Embozene. Three of the studies included by Embozene were unpublished conference reports. The GAE resulted in considerably improved VAS and WOMAC pain levels, as well as improved functional status. There were no significant differences between embolic agents in terms of post-procedural pain relief or functional improvement.

Casadaban et al. (2021) conducted a meta-analysis comprised of three single-arm studies reporting on 186 knees in 133 patients with mild-to-moderate (174/186; 94%) or severe (12/186; 15%) OA. GAE was conducted on 159/186 knees with imipenem/cilastatin and 27/186 knees with Embozene. The authors evaluated the outcomes of Embozene (n=27) and imipenem/cilastatin (n=147) in patients with mild-to-moderate OA and found a larger mean drop in VAS ratings at 1 month for Embozene. Nonetheless, by 6 months, VAS outcomes were comparable. Similar patterns were observed for WOMAC scores, with a 1-month mean drop of 32.2 (Embozene) versus 18.5 (imipenem/cilastatin) and a 6-month mean decrease of 30.0 versus 31.3. Overall, the analysis found that GAE with either agent demonstrated durable clinical responses for mild-to-moderate OA pain.The authors concluded that limited single-arm studies reported that GAE is promising for treating OA-related pain. The majority of mild-to-moderate OA treatments demonstrated long-term clinical responses ranging from 6 months to 4 years. Limited data for severe OA suggests a non-durable response. The researchers noted that future studies should be standardized to facilitate comparison and control for the placebo effect.

National and Specialty Organizations

The **Society of Interventional Radiology (SIR) Foundation** convened an RCP for the development of a research agenda on the percutaneous management of knee OA. The panel was composed of a multidisciplinary group of experts from orthopedic surgery, rheumatology, anesthesiology/pain management, sports medicine, and interventional radiology. A statement on percutaneous management of knee OA issued by the panel on June 2021 noted that "limited published data available suggest that GAE is effective in reducing knee pain from OA" and that GAE will require additional safety and efficacy data to confirm its role in the management algorithm for knee OA (Ahmed et al., 2021).

The **National Institute for Health and Clinical Excellence (NICE)** (2021) concluded that the evidence on the safety of GAE for pain from knee OA shows no major safety concerns in the short term; however, evidence on its efficacy and long-term safety is inadequate in quality and quantity; therefore, the procedure should only be used in the context of research and should only be performed by interventional radiologists with specific training in this technique. NICE recommended that the research includes randomized controlled trials versus shams, as well as current best practices. In addition, the research should report details of patient selection and identify those who would most benefit from this procedure. It should also report details of the technique used, long-term safety, and patient-reported outcomes.

SUPPLEMENTAL INFORMATION

Visual Analog Scale (VAS). The intensity of pain in patients with OA is assessed by using a VAS consisting of a 10 cm-long (100 mm) horizontal line marked with “no pain” on one end and “worst pain imaginable” on the other end. The patients marked the position on the provided line that corresponds best to their level of pain. The numerical values on the VAS were obtained as the distance in centimeters or millimeters from “no pain” to the point marked on the line by each patient.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). A 24-item, condition-specific questionnaire is to be used for hip and knee OA. WOMAC is a self-administered health status measure that assesses the dimensions of pain, stiffness, and function (either separately or as an overall index) in patients with OA of the hip or knee. It is available in 5-point Likert, 11-point numerical rating, and 100-mm VAS formats. The WOMAC consists of three subscales: pain (5 questions), stiffness (2 questions), and physical function (17 questions). The subscale scores can vary, with pain ranging from 0 to 20 points; stiffness, 0 to 8 points; and physical function, 0 to 68 points. Higher scores represent worse pain, stiffness, and functional limitations.

CODING & BILLING INFORMATION

CPT Codes

CPT	Description
37242	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; arterial, other than hemorrhage or tumor (e.g., congenital or acquired arterial malformations, arteriovenous malformations, arteriovenous fistulas, aneurysms, pseudoaneurysms)
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction

HCPCS Codes – N/A

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

02/08/2023 Policy reviewed. Updated content. Revised verbiage and wording for clarity with no changes in intent or coverage position. Updated references.
02/09/2022 New policy. IRO Peer Review 12/23/2022. Reviewed by practicing physician board-certified in Interventional Radiology.

REFERENCES

Government Agencies

1. Centers for Medicare & Medicaid Services (CMS). Medicare Coverage Database. National Coverage Determination (NCD) [search: (genicular OR geniculate) AND (embolization OR Embozene) AND knee AND (pain OR osteoarthritis)]. Available from CMS.
2. Food and Drug Administration.
   - ClinicalTrials.gov Identifier: NCT04662840. Geniculate nerve ablation vs geniculate artery embolization vs. sham for knee osteoarthritic pain. Available from FDA.
   - ClinicalTrials.gov Identifier: NCT05112926. Effectiveness and safety of embosphere microspheres for embolization of the geniculate artery for the treatment of pain with known moderate to severe knee osteoarthritis. Available from FDA.

Peer Reviewed Publications

1. Bagla S, Piechowiak R, Hartman T, et al. Genicular artery embolization for the treatment of knee pain secondary to osteoarthritis. J Vasc Interv Radiol. 2020 Jul;31(7):1096-1102. Doi: 10.1016/j.jvir.2019.09.018. PMID: 31837946.
2. Bagla S, Piechowiak R, Sajan A, et al. Multicenter randomized sham controlled study of genicular artery embolization for knee pain secondary to osteoarthritis. J Vasc Interv Radiol. 2021 Oct 2:S1051-0443(21)01389-0. doi: 10.1016/j.jvir.2021.09.019. PMID: 34610422.
3. Casadaban LC, Mandell JC, Epelboym Y, et al. Genicular artery embolization for osteoarthritis related knee pain: A systematic review and qualitative analysis of clinical outcomes. Cardiovasc Intervent Radiol. 2021;44(1):1-9.
4. Jalaeian H, Acharya V, Shibuya M, et al. Abstract no. 15: Two-year outcomes of comparing Embosphere microspheres versus imipenem–cilastatin for genicular artery embolization in patients with knee osteoarthritis. 2021: 32(5): S8. 2021 May 01. doi: https://doi.org/10.1016/j.jvir.2021.03.428.
5. Felson DT, Naimark A, Anderson J, et al. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthritis Rheum. 1987;30:914–8.
6. Padia SA, Genshaft S, Blumstein G, et al. Genicular artery embolization for the treatment of symptomatic knee osteoarthritis. JB JS Open Access. 2021;6(4):e21.00085. Published 2021 Oct 21. doi:10.2106/JBJS.OA.21.00085
7. Torkian P, Golzarian J, Chalian M, et al. Osteoarthritis-related knee pain treated with genicular artery embolization: A systematic review and meta-analysis. Orthop J Sports Med. 2021;9(7):23259671211021356.

National and Specialty Organizations

1. National Institute for Health and Care Excellence (NICE). Genicular artery embolization for pain from knee osteoarthritis [IPG708]. Published October 27, 2021. Available from NICE. Accessed January 2022.
2. Osteoarthritis Research Society International (OARSI). Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019 Nov;27(11):1578-1589. Doi: 10.1016/j.joca.2019.06.011. PMID: 31278997.
3. Society of Interventional Radiology (SIR). Ahmed O, Block J, Mautner K, et al. Percutaneous management of osteoarthritis in the knee: Proceedings from the Society of Interventional Radiology Research Consensus Panel. 2021 March 6. Available from SIR. Accessed January 2022.
4. United States Bone and Joint Initiative: The Burden of Musculoskeletal Diseases in the United States (BMUS), Fourth Edition. Rosemont, IL. Available from USBJI. Accessed January 2022.

Evidence Based Reviews and Publications

1. DynaMed. Osteoarthritis (OA) of the Knee. EBSCO Information Services. Accessed January 6, 2023. Available from DynaMed. Registration and login required.
2. Hayes. Emerging technology report: Genicular Artery Embolization with Embozene Microspheres for Symptomatic Knee Osteoarthritis. Available from: Hayes. Dec 6, 2021. Registration and login required.