

# Molina Clinical Policy

## Genicular Artery Embolization of the Knee for Osteoarthritis

### Policy No. 410

Last Approval: 2/14/2024

Next Review Due By: February 2025



#### 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 date unknown). 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, exercise, 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, 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

Emboic 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, non-resorbable, 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. 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.

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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.

#### 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.

*\*Genicular artery embolization may be covered for **Medicare members** actively enrolled in an approved investigational device exemption study. Please refer to CMS rather than applying this policy.*

#### SUMMARY OF MEDICAL EVIDENCE

Padia et al. (2021) evaluated the safety and efficacy of geniculate artery embolization (GAE) for the treatment of symptomatic knee osteoarthritis (OA) in 40 patients aged 40 to 80 years (median age 69) with moderate to severe knee OA (based on the Kellgren-Lawrence score) 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- $\mu$ m Embozene particles 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 and the baseline symptoms related to knee OA were quantified using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The primary efficacy endpoint was the change in WOMAC score from baseline to 12 months after GAE with clinical success 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  $\geq$  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  $\geq$  75% reduction at 12 months. The median WOMAC score decreased from 52 to 19 at 12 months. Of thirteen 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 were between 49 and 84 years (mean age 59.4 years) and had radiographic knee OA with 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. Adverse events were recorded at all time points. GAE was performed with 75- or 100- $\mu$ m 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 one genicular artery was achieved in 20 of 20 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 and 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.

In a prospective study, a total of 10 patients (15 knees) who had GAE underwent embolization with 100-to 300- $\mu$ m embosphere microsphere particles. They were compared with a cohort of 11 patients (18 knees) who underwent GAE with imipenem-cilastatin. 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

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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 imipenem-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 (Jalaeian et al. 2021).

Torkian et al. (2021) conducted a meta-analysis including 11 studies that reported on 268 knees in 225 patients who were treated with GAE with various embolic agents. Twenty-one patients were treated with polyvinyl alcohol, 13 patients with resorbable microspheres, 72 patients with Embozene, and 119 patients with imipenem-cilastatin. The main outcome measured was the mean difference between pre- and postembolization values of VAS, WOMAC, and the number of patients who consumed analgesic medications for pain relief. Scores of each study were collected at 1 week, 1-, 3-, 6-, 12- and 24-month follow-ups. The mean difference in VAS score at those respective time points were 32, 36.67, 40.75, 42.80, 45.79, and 58 with p-values all < 0.00001. Patient functional status measured by total WOMAC score increased with 73% improvement after 6-months, 79% after 12-months, and 85% after 24-months with p-values < 0.00001. Symptomatic improvement was reported across all studies with no severe or life-threatening complications reported. The meta-analysis concluded that OA treatment by GAE is associated with significant and sustained pain improvement and functional status.

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 knees) or severe (12 knees) OA. GAE was conducted on 159 knees with imipenem/cilastatin and 27 knees with Embozene. The authors evaluated the outcomes of Embozene and imipenem/cilastatin in patients with mild-to-moderate OA and found a larger mean drop in VAS ratings at 1 month for Embozene, but 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.

Taslakian et al. (2023) performed a systematic review and meta-analysis to analyze GAE for treatment of knee OA. Nine studies were included with 270 patients (339 knees), 69% of patients were female, median age of 65 years, and median BMI of 28 kg/m<sup>2</sup>. At baseline, OA characteristics included a median Kellgren-Lawrence score of 2.5, knee pain VAS of 69, and WOMAC score of 54. Studies were excluded if the sample size was less than 10, patients were treated with concomitant surgeries, or if they did not report any outcomes prespecified in the review. Outcomes measured included VAS score for knee pain and WOMAC score. Data was analyzed to determine the minimal clinically important difference (MCID), substantial clinical benefit (SCB), and weighted mean difference (WMD) of scores. The WMD for knee pain VAS score was -37 at 1 month (8 cohorts), -34 at 3 months (7 cohorts), -39 at 6 months (6 cohorts), and -36 at 12 months (5 cohorts) (all p < 0.001 vs. baseline). The WMD for WOMAC Total Score was -28 at 1 month (5 cohorts), -29 at 3 months (4 cohorts), -30 at 6 months (4 cohorts), and -34 at 12 months (2 cohorts) (all p < 0.001 vs. baseline). The improvement in knee OA symptoms ranged from 1.7 to 2.0 MCID units for knee pain and 1.7 to 2.0 units for WOMAC scores. The percentage of patients achieving the MCID was 76%, 78%, 87%, and 78% for knee pain VAS score at 1, 3, 6, and 12 months. The percentage of patients achieving clinical benefit for WOMAC score at 1, 3, 6, and 12 months was 68%, 83%, 86%, and 92% when using MCID and 44%, 60%, 66%, and 78% when using SCB. Adverse events were minimal with 2.0% of patients requiring medication and 0.3% of patients requiring hospitalization. The most common adverse events reported were skin discoloration (11.6%), knee pain (1.2%), access site hematoma (0.6%), and focal skin ulcers (0.3%). Limitation of this review and meta-analysis include heterogeneity in study design, treatments, and outcomes among studies and variation in completeness of data reported. Safety and effectiveness of GAE compared to other knee OA treatments is still unclear. Currently there is limited evidence suggesting GAE is a safe and effective procedure to improve knee OA symptoms.

### **National and Specialty Organizations**

The **Society of Interventional Radiology (SIR) Foundation** convened a research consensus panel 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"

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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. 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.

## CODING & BILLING INFORMATION

### CPT (Current Procedural Terminology) Code

Code	Description
37242	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural road mapping, 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)

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## APPROVAL HISTORY

02/14/2024	Policy reviewed. No changes to coverage criteria. Updated References and Summary of Medical Evidence.
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.

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#### APPENDIX

**Reserved for State specific information.** Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.