Genicular Artery Embolization of the Knee for Osteoarthritis
Policy No. 410
Last Approval: 2/9/2022
Next Review Due By: February 2022

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplement 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 includes 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).

Genicular 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 an 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 through the catheter into these arteries, to embolize the arteries, blocking them and reducing blood supply to the area of inflammation. During the image-guided procedure, images of the patient’s leg can be viewed in real time. After the procedure, patients may experience temporarily increased knee pain, but over the course of several weeks there may be a reduction or elimination of pain. GAE provides another minimally invasive, nonsurgical intervention treatment option for patients with symptomatic knee OA reluctant to undergo or ineligible for surgery.

Regulatory Status

Embolic agents applied in GAE for OA were classified as temporary and permanent embolic agents and include (but 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 hyper vascular 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.
Vascular occlusion procedures for the treatment of osteoarthritis of the knee are not covered by Molina Healthcare. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud, waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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); a pilot study (Bagla et al., 2020; NCT02850068).

Padia et al. (2021) in a prospective open-label study, assessed the safety and efficacy of GAE for the treatment of symptomatic knee OA in 40 patients aged 40 to 80 years (median age of 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. Knee OA severity was grade 2 in 18% of patients, grade 3 in 43%, and grade 4 in 40%. Embolization of the knee was performed 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. Baseline severity of knee pain was assessed by a visual analog scale (VAS) score (ranging from 0 to 10) and baseline symptoms related to knee OA were quantified using the WOMAC. The primary efficacy endpoint was change in WOMAC score from initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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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 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 magnetic resonance imaging before GAE and at 1 month after GAE. OA symptoms were assessed using WOMAC scores and pain was assessing using VAS score (0 to 100 mm). Adverse events were recorded at all timepoints. 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 increase in pain medication use or intra-articular injection. Embolization of at least 1 genicular artery was achieved in 20/20 (100%) patients. The mean GAE procedure time was 81 minutes. Decreases in VAS and WOMAC 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 score decreased from 61 at baseline to 24 at 1 month, 31 at 3 months, and 31 at 6 months). No patients increased 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 true treatment effect versus placebo effect.

Systematic Analysis/Meta-Analyses

Two meta-analyses on GAE evaluated knee OA and include data on Embozene (Torkian et al., 2021; Casabadan et al., 2021). Torkian et al. (2021) conducted a systematic review and meta-analysis to assess the current evidence for the effectiveness and safety of GAE in treatment of OA-related knee pain. The authors noted that this is the first systematic review and meta-analysis to assess this evidence. The results of this meta-analysis indicate that OA treated by GAE using Embozene, polyvinyl alcohol, resorbable microspheres, or imipenem/cilastatin could be generally considered a safe treatment with no serious complications. It could be associated with significant and sustained dramatic pain improvement with better functional status. There is no significant difference between embolic agents in regard to post-GAE pain reduction or functional improvement. To date, no randomized controlled trial has evaluated the efficacy of GAE.

- A systematic literature search was conducted in the PubMed, Web of Science, EMBASE, and Scopus databases to identify studies related to knee OA treated with GAE. Treatment agents were categorized as Embozene, imipenem/cilastatin, resorbable microspheres, and polyvinyl alcohol. The main outcomes were the mean difference (MD) in pre- and postembolization pain based on the VAS or the WOMAC scores as well as changes in the need for pain medication. Random- and fixed-effects models were applied for data analysis. This meta-analysis included 11 studies reporting on 268 knees in 225 patients treated with GAE using various embolic agents; 72 patients received Embozene. Three of the Embozene studies included were unpublished conference reports. GAE resulted in significantly improved VAS and WOMAC pain scores and better functional status. No significant differences between embolic agents in post-procedural pain reduction or functional improvement were found. Therapeutic agents were categorized as embozene, imipenem/cilastatin, resorbable microspheres, and polyvinyl alcohol. The main outcomes were the mean difference in pre- and post-embolization pain based on the VAS or the WOMAC scores as well as changes in the need for pain medication.

- Of 379 initially inspected publications, 11 (N = 225 patients; 268 knees) were included in the final review. The quality of the studies was fair in 8 and poor in 3, categorized according to the National Institutes of Health quality assessment tool. Overall, 119, 72, 13, and 21 patients were treated with imipenem/cilastatin, Embozene,
resorbable microspheres, and polyvinyl alcohol, respectively. Symptomatic improvement was reported in all studies. The pooled effect size, characterized by MD, showed a significant improvement in the VAS and WOMAC pain scores, with better functional status after GAE. GAE resulted in a decreased need for pain medication for knee OA, with a 27%, 65%, and 73% decline in the number of patients who used opioids, nonsteroidal anti-inflammatory drugs, and intra-articular hyaluronic acid injection, respectively. No significant difference between embolic agents was seen with regard to post-GAE pain reduction. No severe or life-threatening complications were reported.

The authors concluded that this systematic review revealed that mild-to-moderate OA treated by GAE using different embolic particles could generally be considered safe, with no reported serious complications. The procedure resulted in significant and sustained pain improvement as well as better functional status in the studies reviewed. However, due to the lack of high-quality trials, further study is needed to examine GAE’s long-term outcomes, its comparative efficacy with other treatment modalities, and its role in the therapeutic approach. The authors noted the systematic review revealed that mild to moderate OA treated by GAE using different embolic particles could generally be considered safe, with no reported serious complications. The procedure resulted in significant and sustained pain improvement as well as better functional status in the studies reviewed. However, because of the lack of high-quality trials, further research is warranted to evaluate the long-term outcomes of GAE, its comparative efficacy with other treatment modalities, and its role in the therapeutic approach.

Casadaban et al. (2021) conducted a systematic review following Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. This meta-analysis included 3 single-arm studies that reported on 186 knees in 133 patients with mild-to-moderate (174/186; 94%) or severe (12/186; 15%) OA. GAE was performed with imipenem/cilastatin in 159/186 knees and Embozene in 27/186 knees. The authors compared outcomes for patients with mild-to-moderate OA for Embozene (n=27) versus imipenem/cilastatin (n=147) and found a greater mean decrease in VAS scores at 1 month for Embozene (mean decrease of 48.8 mm versus 30.8 mm). However, by 6 months, VAS outcomes were similar (mean decrease of 47.1 mm versus 46.2 mm). WOMAC scores showed a similar pattern, with a 1-month mean decrease of 32.2 (Embozene) versus 18.5 imipenem/cilastatin and a mean 6-month 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. Overall, the analysis found that GAE with either agent demonstrated durable clinical responses for mild-to-moderate OA pain. Average WOMAC scores improved from baseline at 1, 3, 4, 6, 12 and 24 months (45.7 at baseline versus 24.0, 31.0, 14.8, 14.6, 8.2 and 6.2). Severe OA in 12 cases showed initially improved VAS; but was not sustained. Minor adverse events (AEs) such as erythema in the region of embolization (21/186, 11%), puncture-site hematoma (18/186, 10%), paresthesia (2/186, 1%) and fever (1/186, 0.5%) were reported. The authors concluded that limited single-arm studies reported GAE is promising for treating OA-related pain. Most treatments performed for mild-to-moderate OA demonstrated durable clinical responses from 6 months to 4 years. Limited data for severe OA suggested a non-durable response. The researchers noted that future studies should be standardized to facilitate comparison and control for placebo effect.

### Professional Society Guidelines

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 recommends that the research should preferably be randomized controlled trials against sham and 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 assessed by using a visual analogue scale, 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 place that corresponds best to their pain intensity on the given line. The numerical values on the VAS were obtained as the distance in centimeter or millimeters from "no pain" to the point marked on the line by each patient.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). 24-item, condition-specific questionnaire 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 visual analogue scale (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

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
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<tbody>
<tr>
<td>37241</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (e.g., congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicocoeles)</td>
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<tr>
<td>37242</td>
<td>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)</td>
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<tr>
<td>37243</td>
<td>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</td>
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<tr>
<td>37244</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for arterial or venous hemorrhage or lymphatic extravasation</td>
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HCPCS Codes – N/A

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APPROVAL HISTORY

REFERENCES

Government Agencies
2. Food and Drug Administration.
   - ClinicalTrials.gov Identifier: NCT04662840. Geniculate nerve ablation vs geniculate artery embolization vs. sham for knee osteoarthritis 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

National and Specialty Organizations

Evidence Based Reviews and Publications

APPENDIX

Reserved for State specific information (to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.