Title: Prostatic Artery Embolization (PAE) for Benign Prostatic Hypertrophy (BPH)

Description/Background

Prostatic arterial embolization (PAE) is being evaluated as a minimally invasive procedure for benign prostatic hyperplasia that may help improve urinary symptoms caused by an enlarged prostate without the risk of sexual side effects. Using x-ray guidance, interventional radiologists insert a catheter into an artery in the groin or wrist and advanced it to the arteries supplying blood to the prostate gland. Tiny round particles (microspheres) are injected into the arteries, partially blocking the blood flow to the prostate. This procedure is called embolization. Areas of the prostate which are most affected by benign prostatic hyperplasia (BPH) are deprived of oxygen which results in necrosis of targeted areas. Over months the body’s immune system reabsorbs the dead tissue and replaces it with scar tissue which slowly contracts and results in shrinkage of the prostate which alleviates some of the symptoms associated with BPH.

BPH is a noncancerous enlargement of the prostate gland and is the most common benign tumor found in men. BPH affects many older men and causes lower urinary tract symptoms, including urinary frequency, urgency, and dysuria. Oral medication constitutes the primary nonoperative treatment. Although transurethral resection of the prostate (TURP) is considered the standard BPH treatment for patients who are refractory to medical therapy, it is associated with a high rate of erectile and ejaculatory dysfunctions.

Given the strong association between BPH, lower urinary tract symptoms, sexual dysfunction, and the current standard of care (TURP), minimally invasive therapies, including PAE have been evaluated with the intention to increase voiding domains while minimizing adverse sexual effects in men with BPH.
Regulatory Status

In 2017, Embosphere microspheres (BioSphere Medical, S.A.) was reclassified by the U.S. Food & Drug Administration (FDA) into a Class II device. To classify the Embosphere Microspheres into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. The FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. As a result of this order, immediate marketing of the device, as described in the De Novo request - subject to the general control provisions of the FD&C Act and the special controls identified in the order, was granted.

Indications for use: Embolization of arteriovenous malformation, hypervascular tumors, including symptomatic uterine fibroids, and prostatic arteries for symptomatic benign prostatic hyperplasia (BPH). DEN160040. Product code: NOY

Medical Policy Statement

Prostatic arterial embolization for benign prostatic hyperplasia is experimental/investigational. There is insufficient scientific evidence in the current medical literature regarding the safety and efficacy of this technology or that it improves health outcomes.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT/HCPCS Level II Codes (Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)

Established codes:
N/A

Other codes (investigational, not medically necessary, etc.):
37242

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.
Rationale

Abt et al (2021) compared the efficacy and safety of prostatic arterial embolization (PAE) versus transurethral resection of the prostate (TURP) in the treatment of BPH at a 2-year follow-up in a randomized, open label trial. One-hundred and three participants aged ≥ 40 years with refractory lower urinary tract symptoms secondary to benign prostatic obstruction were evaluated. The mean reduction in International Prostate Symptoms Score after 2 years was 9.21 points after PAE and 12.09 points after TURP (difference of 2.88 [95% confidence interval 0.04-5.72]; p = 0.047). Superiority of TURP was also found for most other patient-reported outcomes except for erectile function. PAE was less effective than TURP regarding the improvement of maximum urinary flow rate (3.9 vs 10.23 ml/s, difference of -6.33 [-10.12 to -2.54]; p < 0.001), reduction of post-void residual urine (62.1 vs 204.0 ml; 141.91 [43.31-240.51]; p = 0.005), and reduction of prostate volume (10.66 vs 30.20 ml; 19.54 [7.70-31.38]; p = 0.005). Adverse events were less frequent after PAE than after TURP (total occurrence n = 43 vs 78, p = 0.005), but the distribution among severity classes was similar. Ten patients (21%) who initially underwent PAE required TURP within 2 years due to unsatisfying clinical outcomes, which prevented further assessment of their outcomes and, therefore, represents a limitation of the study. Authors concluded that although PAE was associated with fewer complications than TURP, inferior improvements in lower urinary tract symptoms secondary to benign prostatic obstruction and a relevant re-treatment rate were found 2 years after PAE when compared with TURP.

Knight et al (2021) conducted a systematic review and meta-analysis to compare prostatic artery embolization to the gold standard of transurethral resection of the prostate for benign prostatic hyperplasia. Six studies with 598 patients were included. TURP was associated with significantly more improvement in maximum urinary flow rate (Qmax) (mean difference = 5.02 mL/s; 95% CI [2.66,7.38]; p < 0.0001; I^2 = 89%), prostate volume (mean difference = 15.59 mL; 95% CI [7.93,23.25]; p < 0.0001; I^2 = 88%), and prostate-specific antigen (PSA) (mean difference = 1.02 ng/mL; 95% CI [0.14,1.89]; p = 0.02; I^2 = 71%) compared to PAE. No significant difference between PAE and TURP was observed for changes in International Prostate Symptoms Score (IPSS), IPSS quality of life (IPSS-QoL), International Index of Erectile Function (IIEF-5), and post-void residual (PVR). PAE was associated with fewer adverse events (AEs) (39.0% vs. 77.7%; p < 0.00001) and shorter hospitalization times (mean difference = -1.94 days; p < 0.00001), but longer procedural times (mean difference = 51.43 min; p = 0.004). Subjective symptom improvement was equivalent between TURP and PAE. While TURP demonstrated larger improvements for some objective parameters, PAE was associated with fewer adverse events and shorter hospitalization times.

Jiang et al (2019) evaluated the differences between TURP and PAE in the treatment of benign prostatic hyperplasia. A total of four studies involving 506 patients were included in the meta-analysis. The pooled data showed that the Qmax was higher in TURP group than PAE with a significant difference (WMD:4.66, 95%CI 2.54 to 6.79, P < 0.05). The postoperative QOL was lower in the TURP than PAE group (WMD: -0.53, 95%CI -0.88 to - 0.18, P < 0.05). The postoperative prostate volume was significantly smaller in the TURP than PAE group (WMD: -8.26, 95%CI -12.64 to - 3.88, P < 0.05). The operative time was significantly shorter in the TURP than PAE group (WMD: -10.55, 95%CI -16.92 to - 4.18, P < 0.05). No significant
difference was found in the postoperative IPSS and complications between TURP and PAE (P > 0.05, WMD: 1.56, 95% CI -0.67 to 3.78, p = 0.05, OR: 1.54, 95% CI 1.00 to 2.38, respectively). TURP was found to achieve improved Qmax and QoL compared to PAE. Therefore, authors concluded that for patients with BPH and lower urinary tract symptoms, TURP was superior to PAE.

Other noted trials compare PAE to placebo effect (Pisco et al 2020), discuss current debates regarding optimal patient evaluation and procedure techniques (Powel et al 2020) or evaluate quality of life measures as they pertain to PAE (Carnevale et al 2013).

**Summary**

There is limited data available on PAE’s safety and long-term effects. Larger comparative studies which evaluate PAE against the gold standard (TURP) are needed and may play an important role in patients in whom medical therapy has failed, who are not candidates for surgery or TURP, or refuse surgical interventions. Further randomized studies and long-term evidence is still needed to evaluate the safety and efficacy of PAE as it relates to benign prostatic hyperplasia. The benefit over risk remains unclear in PAE for BPH, as it is not supported by current data and trial designs.

**Supplemental Information**

American Urological Association guidelines on surgical management of BPH with LUTS do not recommend PAE outside the context of a clinical trial, based on expert opinion of the urology panel. The benefit over risk remains unclear.

Clinical trials which may influence future reviews are listed in Table 1.

<table>
<thead>
<tr>
<th>NCT</th>
<th>Title</th>
<th>Participants</th>
<th>End Date</th>
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<tbody>
<tr>
<td>NCT04879940</td>
<td>Phase II Study to Evaluate the Safety and Efficacy of Prostatic Artery Embolization</td>
<td>26</td>
<td>Aug 2024</td>
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</table>

**Government Regulations**

**National:**

*Medicare National Coverage Determinations Manual 100-3. Chapter 1, Part 4, Section 310. Coverage Determinations: Clinical Trials; Revised 10/03/03*

310.1 - *Routine Costs in Clinical Trials* (Effective July 9, 2007)


Effective for items and services furnished on or after July 9, 2007, Medicare covers the routine costs of qualifying clinical trials including reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. All other Medicare rules apply. See Manual for more information.
The following IDE studies have met CMS’ standards for coverage. Studies with the Category A are approved for coverage of routine services only. Studies with the Category B are approved for coverage of the Category B device and related services, and routine services.

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Sponsor Name</th>
<th>NCT Number</th>
<th>IDE Number</th>
<th>CMS Approval Date</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II Study to Evaluate the Safety and Efficacy of Prostatic Artery Embolization in Patients With Localized Prostate Carcinoma and Obstructive Lower Urinary Tract Symptoms</td>
<td>H. Lee Moffitt Cancer Center and Research Institute</td>
<td>NCT04879940</td>
<td>G210009</td>
<td>2021-09-17</td>
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Local:
N/A

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

**Related Policies**

Aquablation (Transurethral Waterjet Ablation) of the Prostate Prostatic Urethral Lift Procedure for the Treatment of BPH

**References**


The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through November 16, 2021, the date the research was completed.
Joint BCBSM/BCN Medical Policy History

<table>
<thead>
<tr>
<th>Policy Effective Date</th>
<th>BCBSM Signature Date</th>
<th>BCN Signature Date</th>
<th>Comments</th>
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<td>5/1/22</td>
<td>2/15/22</td>
<td></td>
<td>Joint policy established</td>
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</table>

Next Review Date: 1st Qtr, 2023
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PROSTATIC ARTERY EMBOLIZATION (PAE) FOR BENIGN PROSTATIC HYPERTROPHY (BPH)

I. Coverage Determination:

<table>
<thead>
<tr>
<th>Coverage Type</th>
<th>Coverage Details</th>
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<tbody>
<tr>
<td>Commercial HMO (includes Self-Funded groups unless otherwise specified)</td>
<td>Not covered</td>
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<tr>
<td>BCNA (Medicare Advantage)</td>
<td>Refer to the Medicare information under the Government Regulations section of this policy.</td>
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<tr>
<td>BCN65 (Medicare Complementary)</td>
<td>Coinsurance covered if primary Medicare covers the service.</td>
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II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- *Duplicate (back-up) equipment is not a covered benefit.*