Medical Policy



Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.

*Current Policy Effective Date: 5/1/24 (See policy history boxes for previous effective dates)

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

Description/Background

Benign prostatic hyperplasia (BPH) is a noncancerous enlargement of the prostate gland. It is the most common benign tumor found in men. The prostate gland is divided into 4 parts consisting of the fibromuscular stroma, and the central, transitional, and peripheral zones. The transitional zone surrounds the prostatic urethra, which is where BPH develops, causing lower urinary tract symptoms (LUTS) and bladder outlet obstruction symptoms including urinary frequency, urgency, and dysuria. The treatment options for LUTS consist of oral drug therapy (primary nonoperative treatment) and surgery. Although transurethral resection of the prostate (TURP) is considered the gold standard for BPH treatment in individuals who are refractory to oral medical therapy, it is associated with a high rate of erectile and ejaculatory dysfunctions.

Prostatic arterial embolization (PAE) is a procedure for benign prostatic hyperplasia that may help improve urinary symptoms caused by an enlarged prostate with minimizing the risk of sexual side effects. Using fluoroscopic 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.

Given the side effects, including sexual dysfunction, seen with the current standard of care (TURP) in treating BPH, minimally invasive therapies, including PAE have been evaluated with the intention to increase voiding domains while minimizing adverse sexual effects in men with BPH. Due to the common origins and anastomoses that the prostatic artery shares with other

important structures and organs, preprocedural evaluation of the vascular prostatic artery and the male pelvis is crucial to assure success and avoid serious complications.

Regulatory Status

In 2017, Embosphere microspheres (aka PAE technology; 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 (PAE) for benign prostatic hyperplasia (BPH) is established. It may be considered a useful therapeutic option when criteria are met.

Prostatic artery embolization for treatment of hematuria of prostatic origin is established. It may be considered a useful option when criteria are met.

Inclusionary and Exclusionary Guidelines

PAE for BPH may be considered established when **ALL** the following are met:

- Selection is done by a multidisciplinary team involving both a urologist and an interventional radiologist
- Gland size 50 grams or greater
- Preserved bladder function

AND ONE of the following are met:

- Moderate to severe lower urinary tract symptoms (LUTS) by International Prostate Symptoms Score (IPSS)^a refractory to medical management^b
- Moderate to severe LUTS in individuals who are poor surgical candidates (e.g., advanced age, multiple comorbidities, or inability to stop anticoagulation or antiplatelet therapy)
- Acute or chronic urinary retention, requiring urinary catheter use.

PAE for hematuria of prostatic origin may be considered medically necessary when one of the following are met:

5-alpha reductase inhibitor(s)^c (ARI) therapy has failed

- Acute bleeding that is uncontrolled with conservative measures
- Recurrent bleeding that is uncontrolled with conservative measures
- ^a IPSS is a reproducible, validated index designed to determine disease severity and response to therapy. Scores range from 0 to 35. Mild (≤7), moderate (8-19), or severe (20-35).
- ^b Documented failure (no clinical improvement after 3 months of therapy), inability to tolerate, or undesirable side effects or pharmacologic intervention for BPH
- ^c Examples consist of finasteride and dutasteride (brand names: Proscar, Propecia, Avodart, and Jalyn)

Note: Procedure should only be done by an interventional radiologist with specific training and expertise in prostatic artery embolization.

Exclusions:

- Bladder cancer
- Catheter dependence over 12 months
- Detrusor/bladder dysfunction
- Gland size < 50 grams
- High-grade prostate cancer/Gleason Score >7
- Large bladder diverticula
- Neurogenic lower urinary tract dysfunction/neurogenic bladder
- Repeat PAE for BPH treatment
- Uncorrectable coagulopathy

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:

37242 37244

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

N/A

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

Dias Jr et al (2021) review the guidelines from the Society of Interventional Radiology and indicate that although PAE for BPH in men with moderate to severe LUTS is a highly effective treatment modality, caution should be applied. Pre- and postprocedural evaluation and training, and standardization of the PAE techniques are crucial to achieve a successful result

and avoid major complications (e.g., transient ischemic proctitis, infarction zones in the pubis, ischemia of the penis glans).

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 patientreported 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; I2 = 89%), prostate volume (mean difference = 15.59 mL; 95% CI [7.93,23.25]; p < 0.00001; I2 = 88%), and prostate-specific antigen (PSA) (mean difference = 1.02 ng/mL; 95% CI [0.14,1.89]; p = 0.02; I2 = 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.

LaRussa et al (2021) created a meta-analysis comparing the outcomes of prostatic artery embolization with photo selective vaporization (PVP), prostatic urethral lift (PUL), and water vapor thermal therapy (WV). Thirty-five publications including 2,653 individuals were included which contained: PVP (13, 949), PUL (9, 577), WV (3, 330), and PAE (10, 728). The international prostate symptom score (IPSS) and the international index of erectile function (IIEF-5) and quality of life (QOL) scores were recorded at baseline, 6 months, and 12 months. At 6 and 12 months, the IPSS and QOL were most improved after PVP, followed by that after PAE, PUL, and, lastly, WV (measured only at 12 months). Between 6 and 12 months, the IPSS and QOL improved with PAE and worsened with PVP and PUL. Only PAE demonstrated statistical improvement in the IIEF-5, which improved from 6 to 12 months. Authors concluded

that PVP and PAE resulted in the largest improvements in the IPSS and QOL. Only PAE resulted in improvement of the IIEF-5.

Sajan et al (2022) completed a meta-analysis via a Medline and Cochran Central database for randomized controlled studies for Rezum, Urolift, Aquablation, and prostatic artery embolization. Variables included the International prostate symptom score (IPSS), maximum urinary flow rate, quality of life, and postvoid residual (PVR). Standard mean differences between treatments were compared using transurethral resection of the prostate (TURP) to assess differences in treatment effect. There was no significant difference in outcomes between therapies for IPSS at the 3, 6, and 12-month follow ups. Although outcomes for Rezum were only available out to 3 months, there were no consistently significant differences in outcomes when comparing Aquablation versus PAE versus Rezum. TURP PVR was significantly better than Urolift at 3, 6, and 12 months. No significant differences in minor or major adverse events were noted. Authors concluded that although significant differences in outcomes were limited, Aquablation and PAE were the most durable at 12 months. PAE has been well studied on multiple randomized control trials with minimal adverse events while Aquablation has limited high quality data and has been associated with bleeding-related complications.

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

Table 1. Key Clinical Trials

NCT	Title	Participants	End Date
NCT04879940	Phase II Study to Evaluate the Safety and Efficacy of Prostatic Artery Embolization in individuals with localized prostate carcinoma and obstructive lower urinary symptoms prior to radiation therapy	26	Aug 2024

Summary

Multiple societies support the use of PAE for BPH when performed by interventional radiology clinicians who are trained in the procedure. Meta-analyses are emerging which indicate that PAE in comparison to other minimally invasive procedures is equivalent or better in regard to complication rates such as bleeding and overall improvements in the QOL, IPSS, and the IIEF-5 scores. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

American Urological Association

American Urological Association updated their guidelines in 2023 to indicate PAE may be offered for the treatment of LUTS/BPH. Recommendations are made that PAE should be performed by clinicians trained in this interventional radiology procedure following a discussion of the potential risks and benefits. (Conditional Recommendation: Evidence level: Grade C).

Surgery is recommended for patients who have renal insufficiency secondary to BPH, refractory urinary retention secondary to BPH, recurrent urinary tract infections (UTIs), recurrent bladder stones or gross hematuria due to BPH, and/or with LUTS/BPH refractory to or unwilling to use other therapies.

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
А	High	 Very confident that the true effect lies close to that of the estimate of the effect
В	Moderate	 Moderately confident in the effect estimate The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
С	Low Very Low	 Confidence in the effect estimate is limited The true effect may be substantially different from the estimate of the effect Very little confidence in the effect estimate The true effect is likely to be substantially different from the
		estimate of effect

National Institute for Health and Care Excellence

NICE (2018) indicates that current evidence on the safety and efficacy of prostate artery embolization for benign prostatic hyperplasia is adequate to support the use of this procedure provided that standard arrangements^a are in place for clinical governance, consent and audit. NICE recommends that candidate selection is done by a urologist and an interventional radiologist and that the procedure is only done by an interventional radiologist with specific training and expertise in prostatic artery embolization. The committee cautions that the evidence shows a relatively high incidence of urinary retention after the procedure and that the procedure involves extensive imaging which may result in significant radiation exposure.

^a Standard arrangements are the most positive recommendation offered by NICE. There is enough evidence for doctors to consider this procedure as an option, although they are not obligated to do so. Discussion should be had with the individual before a decision is made.

Society of Interventional Radiology Multisociety Consensus Position Statement From the Society of Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, Societe Française de Radiologie, and the British Society of Interventional Radiology

The Society of Interventional Radiology Multi-society Consensus Position Statement (2019) on prostatic artery embolization for treatment of lower urinary tract symptoms attributed to benign prostatic hyperplasia has been endorsed by the Asia Pacific Society of Cardiovascular and Interventional Radiology, Canadian Association for Interventional Radiology, Chinese College of Interventionalists, Interventional Radiology Society of Australasia, Japanese Society of Interventional Radiology, and Korean Society of Interventional Radiology. Recommendations are as follows:

Recommendations for PAE

Recommendation	Level of Evidence	Strength of Recommendation
Acceptable minimally invasive treatment option for appropriately selected men with BPH and moderate to severe LUTS	В	Strong
Treatment option in men with BPH and moderate to severe LUTS who have a large prostate gland (>80 cm³), without an upper limit of prostate size	С	Moderate
Treatment option in men with BPH and acute or chronic urinary retention who wish to preserve bladder function as a method of achieving independence from catheter use	С	Moderate
Treatment option in men with BPH and moderate to severe LUTS who wish to preserve erectile and/or ejaculatory function	С	Weak
Treatment option in men with hematuria of prostatic origin as a method of	D	Strong

achieving cessation of bleeding		
Treatment option in men with BPH and moderate to severe LUTS who are deemed not to be candidates for surgery for any of the following reasons: advanced age, multiple comorbidities, coagulopathy, or inability to stop anticoagulation or antiplatelet therapy	E	Moderate
PAE should be included in the individualized patient-centered discussion regarding treatment options for BPH with LUTS	E	Strong
Interventional radiologists, given their knowledge of arterial anatomy, advanced microcatheter techniques, and expertise in embolization procedures, are the specialists best suited for the performance of PAE	Е	Strong
LUTS = lower urinary tract symptoms, PAE = prostatic artery embolization.		

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)

(Rev. 173, Issued: 09-04-14, Effective: Upon Implementation: of ICD-10,

Implementation: Upon Implementation of ICD-10)

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.

Study Title	Sponsor Name	NCT Number	IDE Number	CMS Approval Date	Category
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	H. Lee Moffitt Cancer Center and Research Institute	NCT04879940	G210009	2021-09-17	В

Multiple studies remain on site as active however, the clinical trial site shows them as completed/terminated. They include the following:

NCT Number	Study Title	N	Dates
NCT02930889	Prostate Artery Embolization (PAE) for Lower Urinary Tract Symptoms	21	Oct 2020
	(LUTS) Due to Benign Prostatic Hyperplasia (BPH)		completed
NCT03055624	Prostate Artery Embolization for the Treatment of Symptomatic Benign	9	Feb 2019
	Prostatic Hyperplasia		completed
NCT02592473	Prostate Artery Embolization Safety and Efficacy: A Pilot Study	50	Nov 2021
			Unknown

NCT02396420	Phase II, Single Center, Single Arm, Open Label Investigation of Prostate	2	Jun 2018
	Artery Embolization as a Treatment for Benign Prostatic Hyperplasia in		Terminated
	Men With Prostates Larger Than 90 Grams		

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

- 1. Abt D, Müllhaupt G, Hechelhammer L, et al. Prostatic Artery Embolisation Versus Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia: 2-yr Outcomes of a Randomised, Open-label, Single-centre Trial. Eur Urol 2021; 80:34. PMID 33612376
- Centers for Medicare & Medicaid Services. Coverage Determinations 100-3. Medicare National Coverage Determinations Manual. 2007. 1:4(310). https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=1&ncdver=2&fromdb=true. Accessed December 14, 2022.
- Centers for Medicare and Medicaid Services. Medicare Coverage Related to Investigational Device Exemption (IDE) Studies: Approved IDE Studies. https://www.cms.gov/Medicare/Coverage/IDE/Approved-IDE-Studies. Accessed December 14, 2022
- 4. Dias Jr, US., Liberato de Moura, MR., Cavalcante Viana, PC., Moreira de Assis, A., et al. "Prostatic Artery Embolization: Indications, Preparation, Techniques, Imaging Evaluation, Reporting, and Complications." *RadioGraphics* 2021 41:5, 1509-1530.
- 5. Knight GM, Talwar A, Salem R, Mouli S. Systematic Review and Meta-analysis Comparing Prostatic Artery Embolization to Gold-Standard Transurethral Resection of the Prostate for Benign Prostatic Hyperplasia. Cardiovasc Intervent Radiol. 2021 Feb;44(2):183-193. doi: 10.1007/s00270-020-02657-5. Epub 2020 Oct 19. PMID: 33078236.
- LaRussa S, Pantuck M, Wilcox Vanden Berg R, et al. "Symptomatic Improvement of Lower Urinary Tract Symptoms of Benign Prostatic Hyperplasia: A Comparative Systematic Review and Meta-Analysis of 4 Different Minimally Invasive Therapies." J Vasc Interv Radiol. 2021 Sep;32(9):1328-1340.e11. doi: 10.1016/j.jvir.2021.06.019. Epub 2021 Jul 10. PMID: 34256123.
- 7. Lerner, LB., Barry, MJ., Das, AK. et al. "Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Amendment 2023." *J Urol.* 2023;10.1097/JU.0000000000003698. https://doi.org/10.1097/JU.0000000000003698. Accessed November 29, 2023.

- 8. McWilliams, JP., Bilhim TA., Carneale FC. et al. "Society of Interventional Radiology Multisociety Consensus Position Statement on Prostatic Artery Embolization for Treatment of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: From the Society of Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, Societe Française de Radiologie, and the British Society of Interventional Radiology." J Vasc Interv Radiol 2019; 30:627–637.
- 9. National Institute for Health and Care Excellence. "Interventional procedure recommendations." 2023. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/interventional-procedures-guidance/recommendations. Accessed November 29, 2023.
- National Institute for Health and Care Excellence. Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia. 2018. https://www.nice.org.uk/guidance/ipg611/resources/prostate-artery-embolisation-for-lower-urinary-tract-symptoms-caused-by-benign-prostatic-hyperplasia-pdf-1899873917137861. Accessed November 29, 2023.
- National Institute of Health U.S. National Library of Medicine. Phase II Study to Evaluate the Safety and Efficacy of Prostatic Artery Embolization. 2021. https://clinicaltrials.gov/ct2/show/NCT04879940?term=NCT04879940&draw=2&rank=1. Accessed November 29, 2023.
- 12. Sajan A, Mehta T, Desai P, Isaacson A, Bagla S. "Minimally Invasive Treatments for Benign Prostatic Hyperplasia: Systematic Review and Network Meta-Analysis." *J Vasc Interv Radiol.* 2022 Apr;33(4):359-367.e8. doi: 10.1016/j.jvir.2021.12.029. Epub 2021 Dec 27. PMID: 34968671.
- 13. U.S. Food & Drug Administration. DEN160040: Embosphere Microspheres. 2017. https://www.accessdata.fda.gov/cdrh_docs/pdf16/DEN160040.pdf. Accessed November 29, 2023.
- U.S. Food & Drug Administration. Device Classification Under Section 513(f)(2)(De Novo). Agents, Embolic for treatment of benign prostatic hyperplasia. 2017. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN160040. Accessed November 29, 2023.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 25, 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/22	2/15/22		Joint policy established
5/1/23	2/21/23		Routine maintenance (slp)Vendor Managed: N/A
5/1/24	2/28/24		 Routine maintenance (slp) Vendor Managed: N/A Stance converted from EI to EST 37242 moved to EST 37244 added as EST

Next Review Date: 1st Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE POLICY: PROSTATIC ARTERY EMBOLIZATION (PAE) FOR BENIGN PROSTATIC HYPERTROPHY (BPH)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered
BCNA (Medicare	Refer to the Medicare information under the Government
Advantage)	Regulations section of this policy.
BCN65 (Medicare	Coinsurance covered if primary Medicare covers the
Complementary)	service.

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.