7.01.151	Prostatic Urethral Lift		
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Section:	7.0 Surgery	**Page:**	Page 1 of 35

Policy Statement

Use of prostatic urethral lift (PUL) in individuals with moderate-to-severe lower urinary tract obstruction due to benign prostatic hyperplasia may be considered **medically necessary** when **all** of the following criteria are met:

- Patient has persistent or progressive lower urinary tract symptoms despite medical therapy (α_1-adrenergic antagonists maximally titrated, 5α-reductase inhibitors, or combination medication therapy maximally titrated) over a trial period of no less than 6 months, or is unable to tolerate medical therapy
- Prostate gland volume is less than or equal to 80 milliliter (mL)
- Prostate anatomy demonstrates normal bladder neck without an obstructive or protruding median lobe (i.e., cystourethrogram that shows absence of stones, strictures or tumors)
- Patient does not have urinary retention, urinary tract infection, or recent prostatitis (within past year)
- Patient has had appropriate testing to exclude diagnosis of prostate cancer (see Policy Guidelines section)
- Patient does not have a known allergy to nickel, titanium and/or stainless steel

Use of prostatic urethral lift in **all** other situations is considered **investigational**.

Policy Guidelines

Prostate cancer testing: Prostate Specific Antigen (PSA) test results less than 3 nanograms per milliliter (ng/ml) is generally thought to represent low risk for prostate cancer. Levels at or above 3 ng/ml can have false positives and may not accurately reflect high risk, so additional testing may be needed (e.g., prostate biopsy, ultrasound, digital rectal exam)

The following CPT codes are specific to the NeoTract UroLift® System:

- **52441:** Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant
- **52442:** Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)

The following HCPCS codes may also be billed for the NeoTract UroLift® System:

- **C9739:** Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants
- **C9740:** Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants

Note: CPT codes 52441 and 52442 may not be billed with HCPCS codes C9739 and C9740.

Description

Benign prostatic hyperplasia (BPH) is a common condition in older individuals that can lead to increased urinary frequency, an urgency to urinate, a hesitancy to urinate, nocturia, and a weak stream when urinating. The prostatic urethral lift (PUL) procedure involves the insertion of one or more permanent implants into the prostate, which retracts prostatic tissue and maintains an expanded urethral lumen.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

One implantable transprostatic tissue retractor system has been cleared for marketing by the Food and Drug Administration (FDA) through the 510(k) process. In 2013, the NeoTract UroLift® System UL400 (NeoTract) was cleared (after receiving clearance through the FDA's de novo classification process in March 2013; K130651/DEN130023). In 2016, the FDA determined that the UL500 was substantially equivalent to existing devices (UL400) for the treatment of symptoms of urinary flow obstruction secondary to BPH in individuals ages 50 years and older. In 2017, the FDA expanded the indication for the UL400 and UL500 to include *lateral and median* lobe hyperplasia in men 45 years or older. FDA product code: PEW.

Rationale

Background
Benign Prostatic Hyperplasia
BPH is a common disorder among older individuals that results from hyperplastic nodules in the periurethral or transitional zone of the prostate. BPH prevalence increases with age and is present in more than 80% of individuals ages 70 to 79.[1,] The clinical manifestations of BPH include increased urinary frequency, nocturia, urgency or hesitancy to urinate, and a weak stream when urinating. The urinary tract symptoms often progress with worsening hypertrophy and may lead to acute urinary retention, incontinence, renal insufficiency, and/or urinary tract infection.

Two scores are widely used to evaluate BPH-related symptoms: the American Urological Association Symptom Index (AUASI) and the International Prostate Symptom Score (IPSS). The AUASI is a self-administered 7-item questionnaire assessing the severity of various urinary symptoms.[2,] Total AUASI scores range from 0 to 35, with overall severity categorized as mild (≤7), moderate (8-19), or severe (20-35).[1,] The IPSS incorporates questions from the AUASI and a quality of life question or a "Bother score."[3,,]

Management
Evaluation and management of BPH include assessment for other causes of lower urinary tract dysfunction (e.g., prostate cancer), symptom severity, and the degree that symptoms are bothersome to determine the therapeutic approach.

Medical Therapy
A discussion about medical therapy is generally indicated for patients with moderate-to-severe symptoms (e.g., an AUASI score of ≥8), bothersome symptoms, or both. Available medical

therapies for BPH-related lower urinary tract dysfunction include α-adrenergic blockers (e.g., alfuzosin, doxazosin, tamsulosin, terazosin, silodosin), 5α-reductase inhibitors (e.g., finasteride, dutasteride), combination α-adrenergic blockers and 5α-reductase inhibitors, anti-muscarinic agents (e.g., darifenacin, solifenacin, oxybutynin), and phosphodiesterase-5 inhibitors (e.g., tadalafil).[1,] In a meta-analysis of both indirect comparisons from placebo-controlled studies (including 6333 patients) and direct comparative studies (including 507 patients), Djavan et al (1999) found that the IPSS improved by 30% to 40% and the Qmax score (mean peak urinary flow rate) improved by 16% to 25% in individuals assigned to α-adrenergic blockers.[4,] Combination therapy using an α-adrenergic blocker and 5α-reductase inhibitor has been shown to be more effective for improving IPSS than either treatment alone, with median scores improving by more than 40% over 1 year and by more than 45% over 4 years.[5,]

Surgical and Ablative Therapies

Patients who do not have sufficient response to medical therapy, or who are experiencing significant side effects with medical therapy, may be referred for surgical or ablative therapies. Various surgical and ablative procedures are used to treat BPH. Transurethral resection of the prostate is generally considered the reference standard for comparisons of BPH procedures.[6,] In the perioperative period, transurethral resection of the prostate is associated with risks of any operative procedure (e.g., anesthesia risks, blood loss). Although short-term mortality risks are generally low, a large prospective study with 10654 patients by Reich et al (2008) reported the following short-term complications: "failure to void (5.8%), surgical revision (5.6%), significant urinary tract infection (3.6%), bleeding requiring transfusions (2.9%), and transurethral resection syndrome (1.4%)."[7,] Incidental carcinoma of the prostate was diagnosed by histologic examination in 9.8% of patients. In the longer term, transurethral resection of the prostate is associated with increased risk of sexual dysfunction and incontinence.

Several minimally invasive prostate ablation procedures are available, including transurethral microwave thermotherapy, transurethral needle ablation of the prostate, urethromicroablation phototherapy, and photo selective vaporization of the prostate. The minimally invasive procedures were individually compared with transurethral resection of the prostate at the time they were developed, which provided a general benchmark for evaluating those procedures.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Prostatic Urethral Lift

Clinical Context and Therapy Purpose

The purpose of PUL in patients who have lower urinary tract symptoms due to benign prostatic hyperplasia (BPH) is to provide a treatment option that is an alternative to or an improvement on existing therapies such as medical management or transurethral resection of the prostate (TURP).

The question addressed in this evidence review is: Does PUL improve the net health outcome in individuals with BPH?

The following PICOs were used to select literature to inform this review.

Patients

The relevant population of interest are men who are experiencing lower urinary tract symptoms without a history suggesting non-BPH causes of the symptoms and who do not have sufficient response to medical therapy or are experiencing significant side effects with medical therapy.

Interventions

The therapy being considered is PUL. The PUL procedure involves the placement of one or more implants in lobes of the prostate using a transurethral delivery device. The implant device is designed to retract the prostate to allow expansion of the prostatic urethra. The implants are retained in the prostate to maintain an expanded urethral lumen.

One device, the NeoTract UroLift System, has been cleared for marketing by the U.S. Food and Drug Administration (see Regulatory Status section). The device has two main components: the delivery device and the implant. Each delivery device comes preloaded with a UroLift implant.

Comparators

Various surgical or ablative procedures are used to treat BPH. TURP is generally considered the reference standard for comparisons of BPH procedures. Several minimally invasive prostate ablation procedures have also been developed, including transurethral microwave thermotherapy, transurethral needle ablation of the prostate, urethromicroablation phototherapy, and photo selective vaporization of the prostate.

Outcomes

A number of health status measures are used to evaluate symptoms relevant to BPH and adverse events of treatment for BPH, including urinary symptoms, urinary dysfunction measured by urinary flow rate (Qmax), ejaculatory dysfunction, overall sexual health, and overall QOL. Qmax is measured by uroflowmetry; low rates associated with more voiding dysfunction and rates <10 mL/sec are considered obstructed.

Outcomes data demonstrating durability to at least two years is preferred.

Some validated patient-reported scales are shown in Table 1.

Of note, the prostate volume does not have a direct correlation with the severity of urinary symptoms.[8,]

Table 1. Patient-Reported Health Outcome Measures Relevant to Benign Prostatic Hyperplasia

Populations	Interventions	Comparators	Outcomes
Individuals: • With lower urinary tract obstruction symptoms due to benign prostatic hyperplasia who do not have sufficient response to medical therapy or are experiencing	**Interventions of interest are:** • Prostatic urethral lift	**Comparators of interest are:** • Transurethral resection of the prostate • Minimally invasive prostate resection or ablation • Continued medical management	**Relevant outcomes include:** • Symptoms • Functional outcomes • Health status measures

Populations	Interventions	Comparators	Outcomes
significant side effects with medical therapy			• Quality of life • Treatment-related morbidity
Measure	**Outcome Evaluated**	**Description**	**Clinically Meaningful Difference (If Known)**
Male Sexual Health Questionnaire for Ejaculatory Dysfunction[9,]	Ejaculatory function and quality of life	Patient-administered, 4-item scale. Symptoms rated as absent (15) to severe (0). QOL assessed as no problem (0) to extremely bothered (5).	
Sexual Health Inventory for Men[10,]	Erectile function	Patient-administered, 5-item scale. Erectile dysfunction rated as severe (1-7), moderate (8-11), mild to moderate (12-16), or mild (17-21). Fewest symptoms present for patients with scores 22-25.	5-point change[11,]
American Urological Association Symptom Index; International Prostate Symptom Score[1,3,12,]	Severity of lower urinary tract symptoms	• Patient-administered, 7-item scale. Symptoms rated as mild (0-7), moderate (8-19), or severe (20-35) • IPSS asks an additional question, rating QOL as delighted (0) to terrible (6)	• Minimum of 3-point change[1,12,] • Minimum of 30% change[13,]
Benign Prostatic Hyperplasia Impact Index[14,15,]	Effect of urinary symptoms on health domains	Patient-administered, 4-item scale. Symptoms rated as absent (0) to severe (13).	Minimum of 0.4-point change[12,]

IPSS: International Prostate Symptom Score; QOL: quality of life.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews

Several systematic reviews on PUL have been published. They include a similar set of trials and noncomparative studies. The overlap of studies is shown in Appendix Table 3. Perera et al (2015) reported on the results of a systematic review and meta-analysis[16,] of studies reporting outcomes after the PUL procedure, which included 7 prospective cohort studies,[17,18,19,20,21,22,23,] a crossover study (Cantwell et al [2014][24,]), and the LIFT RCT (Roehrborn et al [2013],[25,] McVary et al [2014][26,]). Shore (2015)[27,] performed a systematic review of UroLift studies, which included the LIFT RCT (Roehrborn et al [2013][25,]; Roehrborn et al [2015][28,]; McVary et al [2014][26,]), a crossover study (Cantwell et al [2014][24,]), and 4 prospective cohort studies (Garrido Abad et al [2013][17,]; Chin et al [2012][21,]; Woo et al [2012][22,]; McNicholas et al [2013][20,]). Jones et al (2016) performed a systematic review of UroLift studies with at least 12 months of follow-up.[29,]Seven studies were identified, which included 4 noncomparative studies (Woo et al [2011],[23,] Chin et al [2012],[21,] McNicholas et al [2013],[20,] Bozkurt et al [2016][30,]), a crossover study (Cantwell et al [2014][24,]), and 2 RCTs (LIFT[25,] and BPH6[11,]). The National Institute for Health and Care Excellence (2016) published technical guidance on prostatic lift procedures.[31,] The National Institute for Care Excellence

performed a literature search and data synthesis to support the development of the guidance. Studies selected were the same studies included in Perera et al (2015),[16] except for the exclusion of Hoffman et al (2012)[18] in the analysis.

Perera et al (2015), Shore (2015) and Jones et al (2016) analyzed data from the PUL arms of the studies only and the National Institute for Health and Care Excellence review was published before the BPH6 RCT. Therefore, these systematic reviews s will not be discussed further.

Jung et al (2019) published a Cochrane systematic review of PUL parallel-group RCTs published up to Jan 2019.[32]. The 2 included RCTs (n=297) were the LIFT and BPH6 trials described in detail in the following section.[25,33] The two RCTs included different comparators and results were not combined meta-analytically. The authors used the GRADE approach to rate the certainty of the evidence. The conclusions were as follows:

- PUL appears less effective than TURP in improving urological symptoms, both in the short-term and long-term (low-certainty evidence)
- PUL may result in a similar QOL compared to TURP (low-certainty evidence)
- PUL may result in similar erectile function compared to TURP (moderate-certainty evidence)
- PUL may result in better ejaculatory function compared to TURP (moderate-certainty evidence)
- Rates of major adverse events are unclear (very low-certainty evidence)
- Rates of retreatment are unclear (very low-certainty evidence)

Randomized Controlled Trials

Two RCTs of PUL have been performed. Key trial characteristics and study results are shown below in Tables 2 and 3, 6 and 7. Additionally, a brief description of each trial is provided in the following sections.

Table 2. PUL Randomized Controlled Trial Characteristics

Study; Trial	Countries	Sites	Dates	Inclusion Criteria		Interventions, n	
					Baseline Prostate Volume, cm^3	Active	Comparator
Sonksen et al (2015)[11]; BPH6	Denmark, Germany, U.K.	10	Feb 2012-Oct 2013	Age ≥50 y, IPSS >12, prostate volume ≤ 60 cm^3, without median lobe obstruction	16-59	PUL=46	TURP=45

Study; Trial	Countries	Sites	Dates	Inclusion Criteria		Interventions, n	
Roehrborn et al (2013)[25]; LIFT	U.S., Canada, Australia	19	Feb-Dec 2011	Age ≥50 y, IPSS ≥13, prostate volume 30-80 cm^3, washed out of BPH medications, without median lobe obstruction	30-77	PUL=140	Sham=66

BPH: benign prostatic hypertrophy; IPSS: International Prostate Symptom Score; PUL: prostatic urethral lift; TURP: transurethral resection of the prostate.

BPH6 Study

Sonksen et al (2015) reported on the results of a multicenter RCT comparing the PUL procedure with TURP among individuals ages 50 and older with lower urinary tract symptoms, secondary to benign prostatic obstruction.[11] Eligible patients had an IPSS above 12, a Qmax of 15 mL/s or less for a 125-mL voided volume, a postvoid residual volume less than 350 mL, and prostate volume of 60 cm^3 or less on ultrasound. Patients were excluded if there was a median lobe obstruction in the prostate or signs of active infection. The trial used a novel composite endpoint, referred to as the BPH6, which included the following criteria:

- Lower urinary tract symptom relief: Reduction in IPSS by ≥30% within 12 months, relative to baseline
- Recovery experience: Self-assessed by patients as ≥70% within 1 month, using a visual analog scale
- Erectile function: Reduction in Sexual Health Inventory for Men (SHIM) score by ≤6 points within 12 months, relative to baseline
- Ejaculatory function: Emission of semen as assessed by question 3 in the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD)
- Continence preservation: Incontinence Severity Index ≤4 points at all follow-up visits
- Safety: No treatment-related adverse events exceeding grade 1 on the Clavien-Dindo classification system at time or procedure or any follow-up

Patients were considered treatment responders if they met all six composite criteria. While this composite endpoint has not been previously validated, core components of the composite score have been independently validated in a clinical setting. The trial used a noninferiority design with a margin of 10% for the primary endpoint, BPH6. Study investigators modified 2 of the original endpoint definitions in the study's analysis, including changing the sexual function element assessment from a single time point (12 months) to assess sustained effects during 12 months of follow-up, and lowering the threshold of quality of recovery on a visual analog scale from 80 to 70.

Table 3. Summary of Evidence From the BPH6 Study

Outcomes	3 Months		12 Months		24 Months	
	PUL	TURP	PUL	TURP	PUL	TURP
Mean change in IPSS						
n	42	34	40	32	37	32
Mean (SD)	-11.7 (8.5)	-11.8 (9.5)	-10.9 (7.9)	-15.4 (6.8)	-9.2 (9.2)	-15.3 (7.5)
p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Comparison (p)	0.978		0.013		0.004	
Change in IPSS QOL						
n	43	34	40	32	37	32
Mean (SD)	-2.6 (1.7)	-2.4 (2.0)	-2.8 (1.8)	-3.1 (1.6)	-2.5 (1.8)	-3.3 (1.6)
p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Comparison (p)	0.55		0.436		0.066	
Change in Qmax						
n	33	25	32	29	27	27
Mean (SD)	4.2 (5.0)	12.7 (9.8)	4.0 (4.8)	13.7 (10.4)	5.0 (5.5)	15.8 (16.5)
p	<0.001	0.003	<0.001	0.003	<0.001	0.002

Outcomes	3 Months		12 Months		24 Months	
Comparison (p)	<0.001		<0.001		0.002	
Change in SHIM score						
n	38	27	32	27	29	28
Mean (SD)	-0.7 (5.2)	-1.0 (5.2)	-0.1 (4.7)	-0.9 (4.3)	-0.2 (4.3)	-1.8 (4.90)
p	0.386	0.328	0.940	0.29	0.832	0.067
Comparison (p)	0.861		0.486		0.201	
Change in MSHQ-EjD function score						
n	38	27	32	27	29	27
Mean (SD)	-0.7 (2.1)	-3.0 (4.1)	1.3 (3.3)	-3.7 (4.1)	0.3 (3.4)	-4.0 (4.6)
p	0.251	<0.001		<0.001	0.666	<0.001
Comparison (p)	<0.001		<0.001		<0.001	
Change in MSHQ-EjD bother score						
n	38	28	32	27	29	27
Mean (SD)	-0.7 (2.1)	0.2 (1.5)	0.5 (2.2)	0.0 (1.5)	-0.1 (2.2)	-0.3 (1.9)
p	0.062	0.470	0.214	0.896	0.734	0.415

Outcomes	3 Months		12 Months		24 Months	
Comparison (p)	0.069		0.359		0.771	
Composite score	NR	NR	Response: 52%	Response: 20%	NR	NR
Comparison (95% CI); p	NR		Difference: 32% (10% to 51%); 0.005		NR	
Clavien-Dindo adverse events						
Grade 1, n (%)	NR	NR	30 (68)	26 (74)	NR	NR
Adverse events			60	79		
Grade 2, n (%)	NR	NR	3 (7)	4 (11)	NR	NR
Adverse events			3	5		
Grade 3, n (%)	NR	NR	4 (9)	5 (14)	NR	NR
Adverse events			4	5		

Adapted from Gratzke et al (2017).[33,]
BPH: benign prostatic hypertrophy; CI: confidence interval; IPSS: International Prostate Symptom Score; MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction; NR: not reported; PUL: prostatic urethral lift; Qmax: mean peak urinary flow rate; QOL: quality of life; SD: standard deviation; SHIM: Sexual Health Inventory for Men; TURP: transurethral resection of the prostate.

Ninety-one patients were randomized to TURP (n=45) or PUL (n=46). Ten patients in the TURP group and 1 patient in the PUL group declined treatment, leaving an analysis group of 80 subjects. The analysis was per-protocol, including 35 in the TURP group and 44 in the PUL group (87% of those randomized; 1 patient was excluded for violating the active urinary retention exclusion criterion). Groups were similar at baseline, except for the MSHQ-EjD function score. For procedure recovery, 82% of the PUL group achieved the recovery endpoint by 1 month compared with 53% of the TURP group (p=0.008). For the study's primary outcome, the proportion of participants who met the original BPH6 primary endpoint was 34.9% for the PUL group, and 8.6% for the TURP group (noninferiority p<0.001; superiority p=0.006). The modified

BPH6 primary endpoint was met by 52.3% of the PUL group and 20.0% of the TURP group (noninferiority p<0.001; superiority p=0.005). Both groups demonstrated improvements over IPSS, IPSS QOL score, BPH-II score, and Qmax over time, as described in Table 3. There were 60 grade 1 adverse events in 30 (68%) PUL patients and 79 adverse events in 26 (74%) TURP patients. The number of patients experiencing grade 2 and 3 adverse events was similar between groups. Intention-to-treat analyses were not reported.

Gratzke et al (2017) reported on 2-year results from BPH6.[33,] Two additional patients were excluded from analysis: one TURP patient who discontinued participation; and one PUL patient who had a protocol violation. Composite scores for the two groups were not reported. Both groups continued to show significant improvements in IPSS score, IPSS QOL, BPH-II score, and Qmax during the two-year follow-up, as described in Table 3. Six (14%) PUL patients and 2 (6%) TURP patients had secondary treatment (PUL, intradetrusor botulinum toxin, laser or TURP procedure), showing moderate durability over 2 years.

The purpose of the limitations tables (see Tables 4 and 5) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 4. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
BPH6	3. Unclear history of BPH treatments			4: Primary outcome was not validated	
LIFT	3. Unclear history of BPH treatments		2: Men were washed out of medication		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
BPH: benign prostatic hypertrophy.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 5. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
BPH6		1. Blinding not feasible		6. Only per-protocol analysis presented		
LIFT				1, 2, 5. High losses and/or exclusions in extended follow-up, only LOCF sensitivity analyses provided		3, 4. CI not reported for treatment effects

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
CI: confidence interval; LOCF: last observation carried forward.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Subsection Summary: BPH6 Study
In the BPH6 study, PUL was both noninferior (p<0.001) and superior (p=0.005) to TURP for the study's composite endpoint. This endpoint was calculated using the concurrent achievement of validated measures of symptoms and complications and is sufficient to describe patient health outcomes. TURP was associated with greater improvements in urinary tract obstruction symptom outcomes and with greater declines in ejaculatory function compared with PUL.

LIFT Study
Comparative Data
Roehrborn et al (2013) reported on results of the pivotal LIFT study, an RCT comparing PUL with sham control among 206 individuals ages 50 and older with lower urinary tract symptoms secondary to BPH.[25] Eligible patients had an American Urological Association Symptom Index (AUASI) score of 13 or greater, Qmax of 12 mL/s or less for a 125-mL voided volume, and a prostate volume between 30 and 80 mL. Patients were excluded if there was median lobe obstruction in the prostate, postvoid obstruction of more than 250 mL, or signs of active infection. Patients underwent washout of BPH medications before enrollment; the washout period was two weeks for α-blockers and three months for 5α-reductase inhibitors. Patients were randomized to PUL (n=140) or sham control (n=66) and evaluated at 3 months postprocedure for the trial's primary efficacy endpoint. After that, all patients were unblinded, and sham control patients were permitted to undergo the PUL procedure. Fifty-three control subjects eventually underwent a PUL procedure. The analysis was intention-to-treat. The study met its primary efficacy endpoint, which was that the reduction in AUASI score at 3 months postprocedure had to be at least 25% greater after the PUL than the reduction in AUASI score seen with sham (p=0.003). The AUASI score decreased from 24.4 at baseline to 18.5 at 3-month follow-up for sham control patients and from 22.2 at baseline to 11.2 at 3-month follow-up for PUL patients (see Table 6). The 3-month change in Qmax was 4.28 mL/s for PUL patients and 1.98 mL/s for sham control patients (p=0.005). Compared with sham control patients, PUL patients had greater improvements in QOL scores and BPH-II score (see Table 7). Nine serious adverse events in seven patients were reported in the PUL group, and one serious adverse event was reported in the sham group during the first three months of follow-up. Limitations in the trial design are summarized in Tables 4 and 5.

McVary et al (2014) reported on sexual function outcomes in a subset of patients from the LIFT study.[26] At baseline, 53 (38%) PUL subjects and 23 (53%) sham control subjects were sexually inactive or had severe erectile dysfunction and were censored from the primary sexual function analysis. Scores on the SHIM, MSHQ-EjD function scale and the MSHQ-EjD bother scale did not differ significantly between groups.

Table 6. Summary of LIFT Initial Trial Results

Study	Change in IPSS	Change in IPSS QOL	Change in Qmax	Change in MSHQ-EjD Function	Change in MSHQ-EjD Bother	Any Adverse Events, n (%)	Serious Adverse Events, n (%)
LIFT							
N at 3 months	206	206	182	144	177	206	206

Study	Change in IPSS	Change in IPSS QOL	Change in Qmax	Change in MSHQ-EjD Function	Change in MSHQ-EjD Bother	Any Adverse Events, n (%)	Serious Adverse Events, n (%)
PUL	-11.1 (7.7)	-2.2 (1.8)	4.3 (5.2)	2.2 (2.5)	-0.8 (1.5)	122 (87%)	7 (5%)
Adverse events						268	9
Sham	-5.9 (7.7)	-1.0 (1.5)	2.0 (4.9)	1.7 (2.6)	-0.7 (1.6)	43 (52%)	1 (1.5%)
Adverse events						53	1
TE (p)	NR (0.003)	NR (<0.001)	NR (0.005)	NR (0.283)	NR (0.60)	NR	NR

Adapted from Roehrborn et al (2013).[25]
Values are mean (standard deviation) unless otherwise indicated.
IPSS: International Prostate Symptom Score; MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction; NR: not reported; PUL: prostatic urethral lift; Qmax: mean peak urinary flow rate; QOL: quality of life; TE: treatment effect.

Table 7. Summary of Evidence for LIFT Study, Including Participants in the PUL Group

Outcomes	3 Months	1 Year	2 Years	3 Years	5 Years
N	140	129	118	109	87
Death/LTFU	0	2	7	2	18
Protocol deviations	3	0	0	1	0
Retreatment	0	6	4	6	4
Change in IPSS					
n	136	123	103	93	72
Change	-11.14 (7.72)	-10.61 (7.51)	-9.13 (7.62)	-8.83 (7.41)	-35.9%
95% CI	-12.45 to -9.83	-11.95 to -9.27	-10.62 to -7.64	-10.35 to -7.30	-44.4% to -27.3%
p	<0.001	<0.001	<0.001	<0.001	<0.001
Change in IPSS QOL					
n	136	123	103	93	72
Change	-2.22 (1.78)	-2.31 (1.60)	2.19 (1.72)	-2.25 (1.72)	-50.3
95% CI	-2.52 to -1.92	-2.59 to -2.02	-2.53 to -1.86	-2.60 to -1.89	-58.4% to -42.2%
p	<0.001	<0.001	<0.001	<0.001	<0.001
Change in Qmax					
n	122	102	86	69	52
Change	4.29 (5.16)	4.03 (4.96)	4.21 (5.09)	3.47 (5.00)	44.3%
95% CI	3.36 to 5.21	3.06 to 5.00	3.12 to 5.30	2.27 to 4.67	29.4% to 59.1%)
p	<0.001	<0.001	<0.001	<0.001	<0.001
Change in SHIM score					
n	91	87	72	66	NR
Change	1.27 (4.65)	0.70 (5.12)	1.06 (4.78)	0.53 (4.41)	NR
95% CI	0.31 to 2.24	-0.39 to 1.79	-0.07 to 2.18	-0.55 to 1.62	NR
p	0.005	0.299	0.046	0.338	NR
Change in MSHQ-EjD function score					
n	91	87	72	66	49
Change	2.31 (2.58)	1.56 (2.68)	1.08 (2.51)	0.56 (2.48)	9.3%
95% CI	1.77 to 2.85	0.99 to 2.13	0.49 to 1.67	-0.05 to 1.17	-3.8% to 22.5%
p	<0.001	<0.001	<0.001	0.013	0.096
Change in MSHQ-EjD bother score					
n	91	87	72	66	49
Change	-1.07 (1.44)	-0.76 (-1.55)	0.63 (1.51)	-0.59 (1.52)	-6.3%

Outcomes	3 Months	1 Year	2 Years	3 Years	5 Years
95% CI	-1.37 to -0.77	-1.09 to -0.43	-0.98 to -0.27	-0.96 to -0.22	-31.5% to 18.8%
p	<0.001	<0.001	<0.001	<0.001	0.019

Adapted from Roehrborn et al (2015)[28] for data from 3 months to 3 years and Roehrborn et al (2017)[34] for data for 5 years.
While not specifically indicated, change values likely represent means and standard deviations.
CI: 95% confidence interval; IPSS: International Prostate Symptom Score; LTFU: lost to follow-up; MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction; NR: not reported; PUL: prostatic urethral lift; Qmax: mean peak urinary flow rate; QOL: quality of life; SHIM: Sexual Health Inventory for Men.

Follow-Up of Sham-Assigned Crossover Participants

Cantwell et al (2014) reported on 12-month outcomes for 53 subjects in the LIFT sham control group who underwent PUL after unblinding at 3 months postprocedure.[24] Crossover (unblinded) patients had a change in IPSS from 23.4 to 12.3 at 3 months postprocedure compared with the change in IPSS from 25.2 to 20.2 at 3 months after the sham procedure. Subjects had greater improvements in BPH-II score in the crossover period (-3.3) than in the sham period (-1.9; p=0.024) but did not report significant differences in improvement in Qmax. Change in sexual function scores did not differ significantly after the sham procedure compared with after the active procedure.

Rukstalis et al (2016) reported on 24-month outcomes for 42 of the 53 participants in the LIFT sham group who underwent PUL after unblinding.[35] During the 24 months, 4 patients were known to have had TURP, and 1 patient required additional PUL implants. The change in IPSS from baseline to 24 months was -9.6 (-35%; 95% CI, not reported; p<0.001) and there were significant score improvements in Qmax, BPH-II scores, and QOL. There were no significant changes compared with baseline for SHIM scores; however, MSHQ-EjD scores improved by 41% (p<0.001).

Follow-Up of PUL-Assigned Participants

Roehrborn et al (2015) reported on 3-year results from patients randomized to PUL in the LIFT study.[28] After exclusion of 11 subjects who were lost to follow-up, 36 subjects with missing data, protocol deviations, medication treatment for BPH, or other prostate procedures, and 15 subjects who underwent surgical retreatment for lower urinary tract symptoms (6 with repeat PUL procedures, 9 with TURP or laser vaporization), the 3-year effectiveness analysis included 93 (66%) of the original 140 subjects. For subjects with follow-up data, change in IPSS was -8.83 (95% CI, -10.35 to -7.30; p<0.001). Significant improvements were also reported for the QOL score, BPH-II score, and Qmax. Sexual function was unchanged. Implants were removed from ten participants. No analyses were performed to assess how sensitive the results were to changes in the assumptions about the considerable amount of missing data.

Roehrborn et al (2016) reported on 4-year results from patients randomized to PUL in the LIFT study.[36] Of the 140 originally randomized patients, 32 were lost by the 4-year follow-up visit (6 losses were deaths). Of the remaining 108 patients for whom data were available, an additional 29 patients were excluded from analysis for BPH retreatment or protocol deviations. For the 79 (56%) of the 140 subjects included in the analysis, change in IPSS score was -8.8 (precision not given) or -41% (95% CI, -49% to -33%; p<0.001). Significant improvements (vs baseline) were also reported for scores relating to the QOL, BPH-II, and Qmax. Authors reported that 14% "of the 140 originally enrolled" participants had surgical retreatment at some point during the 4 years; however, the 4-year follow-up included 79 patients, so the denominator for the 14% is not clear, and estimated retreatment rates are likely underestimated since individuals lost to follow-up could also have received retreatment. Attributes of patients who received retreatment were not analyzed. SHIM scores did not differ statistically from baseline.

Roehrborn et al (2017) reported on 5-year results from patients randomized to PUL in the LIFT study.[34] The authors reported two analyses. The first was called a per-protocol analysis, which censored patients who had additional BPH procedures, started a BPH medication or had a protocol deviation. A second analysis was called intention-to-treat analysis, which used the last

observation carried forward to impute values that were censored in the per-protocol analysis. While there were 104 participants with 5-year data, only 72 patients were included in the per-protocol analysis after exclusion for protocol violations, additional BPH procedures, or treatment with BPH medication. In the intention-to-treat analysis, change in IPSS was -7.85 at 5 years (-35%; 95% CI, -41% to -29%; p<0.001). In the per-protocol analysis, change in IPSS was -7.56 at 5 years (-35.9%; 95% CI, -44% to -27%). Significant improvements, compared with baseline, continued to be reported for scores associated with QOL, Qmax, and BPH-II.

Subsection Summary: LIFT Study
The LIFT RCT compared PUL with a sham procedure in individuals who had completed a washout period for BPH medications before enrollment. The PUL procedure was associated with greater improvements in lower urinary tract symptoms compared with sham; additionally, the PUL procedure was found to have not worsened sexual function after three months of follow-up. After 3 months, patients were given the option to have PUL surgery and about 80% of the sham patients did so. Functional improvements, compared with baseline, appear durable in patients over two years and are consistent with the BPH6 study. Follow-up over three to five years was notable for a high number of patients who were either excluded or lost.

Section Summary: Randomized Controlled Trials
The BPH6 study demonstrated that PUL is noninferior to TURP when assessed by a composite score, which reflects concurrent improvements in validated scales of symptoms, safety, and sexual function. These findings are reflected in the analysis of the individual aspects of the composite score. PUL demonstrates measurable improvements in urinary symptoms to two years and is superior to TURP in preserving ejaculatory function. These findings were confirmed in the LIFT study, which compared PUL with a sham treatment. Prior to crossover at three months, patients were found to have greater improvement in urinary symptoms relative to patients receiving sham treatment and preserved sexual function. After 3 months, 80% of patients who had received a sham treatment chose to have the PUL procedure. Patients treated with PUL had improvement of urinary symptoms with preservation of sexual function, consistent with the BPH6 study. These findings were preserved in a subset of patients over three to five years; a high number of patients were either excluded or lost to follow-up during this time. The BPH6 and LIFT RCTs excluded men with median lobe obstruction.

The published evidence supports a meaningful improvement in the net health outcome. Evidence reported through clinical input further supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice. Selection criteria of patients for whom evidence is sufficient to support improvement are derived from clinical trial eligibility criteria, product labeling, and clinical input. Further details from clinical input are included in the Clinical Input section and the Appendix.

Noncomparative Studies
Several noncomparative studies were published including men without median lobe obstruction. These studies were previously enumerated in the description of the systematic reviews and are shown in Appendix Table 3. Since RCTs with long-term follow-up exist for this population, these noncomparative studies will not be discussed in further detail.

Rukstalis et al (2018) reported results of the MedLift study, the study used to support the expansion of the Food and Drug Administration clearance for PUL to include obstructive median lobes.[37,] MedLift was a single-arm study enrolling 45 men with eligibility criteria identical to LIFT except requiring obstructive median lobes. Results in the MedLift cohort were compared to the LIFT historical cohort. Characteristics are shown in Table 8.and results are shown in Table 9. One patient required surgical retreatment and no implants were removed over the 12 months of follow-up.

Table 8. Summary of Characteristics of Key Non-comparative Studies

Study	Country	Sites	Participants	Treatment Delivery	Follow-Up
Rukstalis (2018)	US	9	n=45 Men ages 50+ with IPSS>13, Qmax <=12 mL/s, 30 to 80 cc intraurethral prostatic volume and, OMLa	UroLift PUL procedure with median lobe deployment	12 months

[a]OML (Obstructive Median Lobe) was defined as excessive posterior tissue that precludes a normal lateral lobe procedure.

Table 9. Summary Results of Key Non-comparative Studies

Study	IPSS	IPSS QOL	Qmax	SHIM
Rukstalis (2018)	At 12 m	At 12 m	At 12 m	At 12 m
n	44	44	37	38
Change from baseline, mean (SD); p-value	-13.5 (7.7); p<0.001	-3.0 (1.5); p<0.001	6.4 (7.4); p<0.001	1.2 (4.3); p=0.04

CI: 95% confidence interval; IPSS: International Prostate Symptom Score; Qmax: mean peak urinary flow rate; QOL: quality of life; SHIM: Sexual Health Inventory for Men; SD: standard deviation.

The purpose of the limitation tables (see Tables 10 and 11) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 10. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Rukstalis (2018)	3. Unclear history of BPH treatments		2: No concurrent comparator	3: Reporting of adverse events was qualitative; rates not reported	1, 2: Only 12 m of follow-up reported

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
BPH: benign prostatic hypertrophy.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 11. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Rukstalis (2018)	1,2: Not randomized	1,2: No blinding		>15% missing data for Qmax and SHIM		3: CIs not reported

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
CI: confidence interval; Qmax: mean peak urinary flow; SHIM: Sexual Health Inventory for Men.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Noncomparative Studies
One single-arm study (n=45) including men with obstructive median lobes has been conducted and was used to support the Food and Drug Administration expansion of the PUL indication to include these men. Symptom scores and QOL appeared to improve by statistically and clinically significant amounts and were similar in magnitude to improvements reported in the original LIFT study. Rates of adverse events were not reported. Design and conduct limitations preclude interpretation.

Summary of Evidence
The following conclusions are based on a review of the evidence, including but not limited to, published evidence and clinical expert opinion, solicited via Blue Cross Blue Shield Association's Clinical Input Process.

For individuals who have lower urinary tract obstruction symptoms due to BPH who do not have sufficient response to medical therapy or are experiencing significant side effects with medical therapy and receive a PUL, the evidence includes systematic reviews, RCTs, and noncomparative studies. The relevant outcomes are symptoms, functional outcomes, health status measures, QOL, and treatment-related morbidity. One RCT, the BPH6 study, compared the PUL procedure with transurethral resection of the prostate and reported that the PUL procedure was noninferior for the study's composite endpoint, which required concurrent fulfillment of six independently validated measures of symptoms, safety, and sexual health. While transurethral resection of the prostate was superior to PUL in managing lower urinary tract symptoms, PUL did provide significant symptom improvement over two years. PUL was further superior to transurethral resection of the prostate in preserving ejaculatory function. These findings were corroborated by another RCT (the LIFT study), which compared PUL with sham control. Patients underwent washout of BPH medications before enrollment. LIFT reported that patients with the PUL procedure, compared with patients who had sham surgery and no BPH medication, had greater improvements in lower urinary tract symptoms without worsened sexual function at three months. After 3 months, patients were given the option to have PUL surgery; 80% of the patients with sham procedures chose that option. Publications from this trial reported that functional improvements were durable over 3-, 4-, and 5-year follow-ups in a subset of patients treated with PUL; there was a high number of exclusions and loss to follow-up in that group. The BPH6 and LIFT RCTs excluded men with median lobe obstruction. The published evidence supports a meaningful improvement in the net health outcome. Evidence reported through clinical input further supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice. Selection criteria of patients for whom evidence is sufficient to support improvement are derived from clinical trial eligibility criteria, product labeling, and clinical input. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Clinical Input
Clinical input is sought to help determine whether the use of prostatic urethral lift (PUL) for individuals with moderate-to-severe lower urinary tract obstruction symptoms due to benign prostatic hyperplasia (BPH) would provide a meaningful clinical benefit, defined as an improved net health outcome and whether this use is consistent with generally accepted medical practice.

Respondents

Clinical input was provided by the following specialty societies and physician members identified by a specialty society or clinical health system:

- John Lin, MD, Urology; identified by American Urological Association (AUA)[a]
- Anonymous, MD, Urology; identified by AUA[a]
- Anonymous, MD, Urology; identified by University of California San Francisco (UCSF) Medical Center
- Anonymous, MD, Urology; identified by UCSF Medical Center

[a] Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix 1).

Clinical input provided by the specialty society at an aggregate level is attributed to the specialty society. Clinical input provided by a physician member designated by a specialty society or health system is attributed to the individual physician and is not a statement from the specialty society or health system. Specialty society and physician respondents participating in the Blue Cross Blue Shield Association (BCBSA) Evidence Street® clinical input process provide review, input, and feedback on topics being evaluated by Evidence Street. However, participation by a specialty society and/or physician member designated by a specialty society or health system in the clinical input process does not imply an endorsement or explicit agreement with the Evidence Opinion published by BCBSA or Blue Shield of California.

Clinical Input Responses

Figure 1:

Clinical Indication	Respondent	Identified by	Confidence Level That Clinical Use Expected to Provide Meaningful Clinical Benefit: Yes or No	NO: High 5	4	3	2	Intermediate 1	YES: Low 1	2	Intermediate 3	4	High 5	Confidence Level that Clinical Use is Consistent with Generally Accepted Medical Practice: Yes or No	NO: High 5	4	3	2	Intermediate 1	YES: Low 1	2	Intermediate 3	4	High 5
PUL for individuals with moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Anonymous*	AUA	YES										■	YES										■
	Dr. Lin*	AUA	YES										■	YES										■
	Anonymous	UCSF Med Ctr.	YES								■			NO			■							
	Anonymous	UCSF Med Ctr.	YES									■		YES								■		
PUL for individuals with moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Anonymous*	AUA	YES										■	YES										■
	Dr. Lin*	AUA	YES										■	YES										■
	Anonymous	UCSF Med Ctr.	YES									■		YES									■	
	Anonymous	UCSF Med Ctr.	YES								■			YES								■		
PUL for individuals with moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Anonymous*	AUA	YES										■	YES										■
	Dr. Lin*	AUA	YES								■			YES								■		
	Anonymous	UCSF Med Ctr.	YES										■	YES										■
	Anonymous	UCSF Med Ctr.	YES									■		YES								■		

AUA: American Urological Association; UCSF Med Ctr: University of California San Francisco Medical Center; PUL: prostatic urethral lift.

* Indicates that information on conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix 1).

Additional Comments

For use of PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms due to BPH and failed medical management:

- "After failure of medical management, I think offering PUL and TURP [transurethral resection of the prostate] would be equivalent. First, the efficacy of PUL appears to be clinically meaningful with fewer attendant risks. Moreover, the durability appears to be comparable to TURP. PUL may be more appropriate for younger patients where concern over erectile dysfunction (ED) and ejaculatory dysfunction may be more important. In addition, the prostate anatomy may impact selection - with a normal bladder neck and

primarily lateral lobe obstruction better candidates for PUL, as well as not massively enlarged prostates." (Anonymous, MD, Urology; identified by UCSF Medical Center)

- "In general patients select PUL after trying medical therapy, but holding this as a criterion for treatment is not recommended by AUA BPH guidelines, nor is it standard practice. There are many reasons certain men may wish to avoid a medication or increasing their polypharmacy, common in this demographic. If a man wishes to continue medical therapy, he is usually returned to the care of his PCP until such time as he wishes to be more definitively treated. This makes sense for my practice and is undoubtedly more efficient quality care within insurance systems. If a man cannot tolerate medical therapy or is responding poorly to medical therapy, PUL is the obvious next line treatment option. It is the least invasive option that offers the most rapid result, the only option to not induce sexual dysfunction, and an option that has been shown to be at least as durable and arguably more durable than heat ablation treatments currently covered..." (Dr. Lin, Urology; identified by AUA)

For use of PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms due to BPH and not a surgical candidate:

- "This is the most likely clinical scenario for PUL, where the risks of TURP outweigh the benefits. We have many patients for whom TURP and the associated anesthesia pose significant risks. Thus, PUL may be the best approach with the ability to perform the procedure under anesthesia, and no risks of bleeding nor electrolyte and fluid abnormalities." (Anonymous, MD, Urology; identified by UCSF Medical Center)
- "This is an important subset patient population that is well-served by PUL, but is already indicated by Indication #1 discussed above. By no means, however, should PUL indication be limited to this very sick population, as the majority of data published support PUL safety and effectiveness in healthier populations of #1. I deliver PUL in my office with minimal anesthesia required, a critical risk for these patients. As bleeding and bladder irrigation are minimized in PUL when compared to other BPH procedures, the risk of post op fluid shifts, transfusion, and readmissions is greatly minimized. There are very few of these patients included in the broad bibliography of clinical studies, but my personal experience has been positive." (Dr. Lin, Urology; identified by AUA)
- "I have used UroLift for failed medical therapies and failed microwave treatments. Good success in patients with short term urinary retention. Ninety percent of such patients are catheter free at 4 weeks. Done most often in office with oral sedation." (Anonymous, MD, Urology; identified by AUA)
- "In short- to medium-term studies, PUL shows improvement in patient symptom score. This provides a meaningful alternative to medical management or transurethral resection/ablation of the prostate. The benefit of PUL is that it can be done under minimal sedation, which provides a possibility of a procedure to benefit patients who have failed or cannot tolerate medical therapy but who are at high risk for general anesthesia. In addition, PUL can be performed safely for patients on anticoagulation, and this provides a significant benefit compared to TURP given that the risk of bleeding from TURP on anticoagulation is high, and this provides an alternative with a lower complication risk in that regard. Finally, the PUL sutures can be later removed during TURP, so this therapy does not preclude a TURP in the future if necessary for improved symptom control." (Anonymous, MD, Urology; identified by UCSF Medical Center)

See Appendices 1 and 2 for details of the clinical input.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2017
In response to requests in 2017, clinical input on the use of a prostatic urethral lift for 3 indications were received from 4 respondents, including 2 physician-level responses identified through a specialty society and 2 physician-level responses identified through an academic medical center. Evidence from clinical input is integrated within the Rationale section summaries and the Summary of Evidence.

Practice Guidelines and Position Statements
National Institute for Health and Care Excellence
The National Institute for Health and Care Excellence (2014) published guidance on urethral lift implants to treat lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).[38,] The guidance stated:

> "Current evidence on the efficacy and safety of insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia is adequate to support the use of this procedure."

The Institute (2015) published guidance on the use of UroLift for treating LUTS of BPH.[39,]The guidance stated: "the UroLift system is effective in relieving symptoms of benign prostatic hyperplasia" and "the UroLift system should be considered as an alternative to current surgical procedures for use in a day-case setting in individuals with lower urinary tract symptoms of benign prostatic hyperplasia who are aged 50 years and older and who have a prostate of less than 100 ml without an obstructing middle lobe."

American Urological Association
The American Urological Association (2018) published guidelines on the surgical management of LUTS attributed to BPH; the 2018 guidelines were amended in 2019.[6,40,41,]The guidelines made the following recommendations and statements regarding prostatic urethral lift (PUL).

- "Clinicians should consider PUL [prostatic urethral lift] as an option for patients with LUTS [lower urinary tract symptoms] attributed to BPH [benign prostatic hyperplasia] provided prostate volume <80g and verified absence of an obstructive middle lobe; however, patients should be informed that symptom reduction and flow rate improvement is less significant compared to TURP [transurethral resection of the prostate]. Patients should be informed that evidence of efficacy and retreatment rates are poorly defined. "
  - "Moderate Recommendation; Evidence Level: Grade C indicating "Benefits > Risks/Burdens (or vice versa); Net benefit (or net harm) appears moderate. Applies to most patients in most circumstances but better evidence is likely to change confidence"
  - "...the quality of evidence for non-serious harms related to the procedure was rated low, while that for incontinence, need for reoperation, and serious harms related to treatment was rated very low."
  - "...patients selecting PUL should be informed that this is a relatively new intervention for LUTS/BPH with uncertainties in long-term durability, though such uncontrolled data are available."
- "PUL may be offered to eligible patients concerned with erectile and ejaculatory function for the treatment of with LUTS attributed to BPH."
  - "Conditional Recommendation; Evidence Level: Grade C indicating "Risks/Burdens unclear; Alternative strategies may be equally reasonable. Better evidence likely to change confidence"

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in June 2019 did not identify any ongoing or unpublished trials that would likely influence this review.

Appendix

Appendix 1: Clinical Input

Appendix Table 1. Respondent Profile

Physician					
No.	**Name**	**Degree**	**Institutional Affiliation**	**Clinical Specialty**	**Board Certification and Fellowship Training**
Identified by American Urological Association					
1	Anonymous	MD	St. Joseph Hospital	Urology	American Board of Urology
2	John C. Lin	MD	Sunrise Urology	Urology	American Board of Urology
Identified by University of California San Francisco Medical Center					
3	Anonymous	MD	University of California San Francisco Medical Center	Urology	American Board of Urology, Endourology and Urologic Oncology
4	Anonymous	MD	University of California San Francisco Medical Center	Urology	American Board of Urology Eligible, Fellowship trained in male reconstruction

Appendix 1 Table 2. Respondent Conflict of Interest Disclosure

No.	**1. Research support related to the topic where clinical input is being sought**		**2. Positions, paid or unpaid, related to the topic where clinical input is being sought**		**3. Reportable, more than $1,000, health care–related assets or sources of income for myself, my spouse, or my dependent children related to the topic where clinical input is being sought**		**4. Reportable, more than $350, gifts or travel reimbursements for myself, my spouse, or my dependent children related to the topic where clinical input is being sought**	
	Yes/ No	**Explanation**	**Yes/ No**	**Explanation**	**Yes/ No**	**Explanation**	**Yes/ No**	**Explanation**
1	No		Yes	Teach UroLift procedure	Yes	Teach UroLift procedure	No	
2	No		Yes	I currently offer the Prostatic Urethral Lift as	No		No	

No.	1. Research support related to the topic where clinical input is being sought		2. Positions, paid or unpaid, related to the topic where clinical input is being sought		3. Reportable, more than $1,000, health care–related assets or sources of income for myself, my spouse, or my dependent children related to the topic where clinical input is being sought		4. Reportable, more than $350, gifts or travel reimbursements for myself, my spouse, or my dependent children related to the topic where clinical input is being sought	
	Yes/ No	Explanation	Yes/ No	Explanation	Yes/ No	Explanation	Yes/ No	Explanation
				part of the standard of care for BPH for essentially all patients, but my patients covered by the Blue Cross Blue Shield plan in my state. I have been designated as a Center of Excellence in this care.				
3	No		No		No		No	
4	No		No		No		No	

Individual physician respondents answered at individual level. Specialty Society respondents provided aggregate information that may be relevant to the group of clinicians who provided input to the Society-level response.
BPH: benign prostatic hyperplasia.

Appendix 2: Clinical Input Responses

Objective:

Benign prostatic hyperplasia is a common condition in older men that can lead to increased urinary frequency, an urgency to urinate, a hesitancy to urinate, nocturia, and a weak stream when urinating. The prostatic urethral lift (PUL) procedure involves the insertion of one or more permanent implants into the prostate, which retracts prostatic tissue and maintains an expanded urethral lumen.

The following PICO applies to this indication.

Populations	Interventions	Comparators	Outcomes
Individuals: • With moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Interventions of interest are: • Prostatic urethral lift	Comparators of interest are: • Medical management • Minimally invasive prostate resection or ablation • Transurethral resection of the prostate	Relevant outcomes include: • Symptoms • Functional outcomes • Health status measures • Quality of life • Treatment-related morbidity
Individuals: • With moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Interventions of interest are: • Prostatic urethral lift	Comparators of interest are: • Minimally invasive prostate resection or ablation	Relevant outcomes include: • Symptoms

Populations	Interventions	Comparators	Outcomes
		• Transurethral resection of the prostate	• Functional outcomes • Health status measures • Quality of life • Treatment-related morbidity
Individuals: • With moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Interventions of interest are: • Prostatic urethral lift	Comparators of interest are: • Minimally invasive prostate resection or ablation • Medical management	Relevant outcomes include: • Symptoms • Functional outcomes • Health status measures • Quality of life • Treatment-related morbidity

Clinical input is sought to help determine whether the use of PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) would provide a meaningful clinical benefit, defined as improved net health outcome, and whether this use is consistent with generally accepted medical practice.

Responses

1. Based on the evidence and your clinical experience, describe for each clinical indication listed below the clinical context that may offer clinical benefit.
    a. Provide supporting rationale and explanation of objective condition characteristics (e.g., patient selection criteria such as American Urological Association Symptom Index or the International Prostate Symptom Score, prostate size, or patient age) and any management criteria (i.e., regarding prior application of standard diagnostic or therapeutic options) for clinical use.
    b. Include any relevant references to support your clinical input.

No.	Indications	Rationale
1	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Used for management of benign prostatic hyperplasia (BPH)
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes
2	PUL for individuals with moderate-to-severe	PUL should be offered under similar criteria to other BPH treatment options. The AUA BPH guidelines state that moderate

No.	Indications	Rationale
	lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	to severe symptoms are AUASI>7 and designate candidacy for all options. While medical therapy should be offered, all treatment options should be discussed, and patients should select the appropriate treatment often relying on how bothered they are by symptoms or current treatment side effects. I routinely treat these patients with PUL with excellent results that reflect those published in numerous studies.
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	In general patients select PUL after trying medical therapy but holding this as a criterion for treatment is not recommended by AUA BPH guidelines, nor is it standard practice. There are many reasons certain men may wish to avoid a medication or increasing their polypharmacy, common in this demographic. If a man wishes to continue medical therapy, he is usually returned to the care of his PCP until such time as he wishes to be more definitively treated. This makes sense for my practice and is undoubtedly more efficient quality care within insurance systems. If a man cannot tolerate medical therapy or is responding poorly to medical therapy, PUL is the obvious next line treatment option. It is the least invasive option that offers the most rapid result, the only option to not induce sexual dysfunction, and an option that has been shown to be at least as durable and arguably more durable than heat ablation treatments currently covered by the plan in my state.
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	6. This is an important subset patient population that is well-served by PUL but is already indicated by Indication #1 discussed above. By no means, however, should PUL indication be limited to this very sick population, as the majority of data published support PUL safety and effectiveness in healthier populations of #1. I deliver PUL in my office with minimal anesthesia required, a critical risk for these patients. As bleeding and bladder irrigation are minimized in PUL when compared to other BPH procedures, the risk of post op fluid shifts, transfusion, and readmissions is greatly minimized. There are very few of these patients included in the broad bibliography of clinical studies, but my personal experience has been positive.
3	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	PUL is reasonable if patients are unable to tolerate initial medical therapy. The benefit of PUL compared to TURP is less invasive procedure with fewer potential complications and side effects. However, I believe that medical therapy would still be first-line intervention.
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	After failure of medical management, I think offering PUL and TURP would be equivalent. First, the efficacy of PUL appears to be clinically meaningful with fewer attendant risks. Moreover, the durability appears to be comparable to TURP. PUL may be more appropriate for younger patients where concern over erectile dysfunction (ED) and ejaculatory dysfunction may be more important. In addition, the prostate anatomy may impact selection - with a normal bladder neck and primarily lateral lobe obstruction better candidates for PUL, as well as not massively enlarged prostates.
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	This is the most likely clinical scenario for PUL, where the risks of TURP outweigh the benefits. We have many patients for whom TURP and the associated anesthesia pose significant risks. Thus, PUL may be the best approach with the ability to perform the procedure under anesthesia, and no risks of bleeding nor electrolyte and fluid abnormalities.
4	PUL for individuals with moderate-to-severe lower urinary tract	Short-term data show symptom improvement based on IPSS symptom score compared with other surgical treatment such as TURP.

No.	Indications	Rationale
	obstruction symptoms (due to benign prostatic hyperplasia)	
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	For patients who have failed medical management or cannot tolerate medical management, PUL offers a good alternative to TURP given that in short-term data it has shown improvement of symptom scores, and has low risk of complications
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	PUL can be performed under minimal or even no sedation, providing a good alternative for patients who cannot tolerate anesthesia for TURP.

2. Based on the evidence and your clinical experience for the indications described in Question 1:
   c. Respond Yes or No for each clinical indication whether the intervention would be expected to provide a meaningful clinical benefit in the net health outcome.
   d. Use the 1 to 5 scale outlined below to indicate your level of confidence that there is adequate evidence that supports your conclusions.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes					X
2	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms	Yes					X

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
	(due to benign prostatic hyperplasia) and failed medical management						
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes			X		
3	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes			X		
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes				X	
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes					X
4	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes				X	
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes			X		
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes				X	

3. Based on the evidence and your clinical experience for the indications described in Question 1:
   a. Respond Yes or No for each indication whether this intervention is consistent with generally accepted medical practice.
   b. Use the 1 to 5 scale outlined below to indicate your level of confidence in your conclusions.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes					X
2	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes					X
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes			X		
3	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	No			X		

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes				X	
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes					X
4	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia)	Yes			X		
	PUL for individuals with moderate to severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and failed medical management	Yes			X		
	PUL for individuals with moderate-to-severe lower urinary tract obstruction symptoms (due to benign prostatic hyperplasia) and not surgical candidate	Yes			X		

4. Additional comments and/or any citations supporting your clinical input on this topic.

No.	Additional Comments
1	I have used UroLift for failed medical therapies and failed microwave treatments. Good success in patients with short term urinary retention. Ninety percent of such patients are catheter free at 4 weeks. Done most often in office with oral sedation.
2	PUL is an important and medically necessary part of my BPH practice for Medicare, United Healthcare, Cigna, Aetna and several out-of-state Blue Cross plans. These insurers have correctly determined that it is advantageous and necessary to offer their beneficiaries access to receiving treatment for BPH without causing potentially permanent damage to their sexual function. They appreciate that outpatient or, in my case, office treatment is more efficient, less costly, and provides better quality of care for their beneficiaries. TURP and laser treatments, the primary BPH procedures performed, are constantly in the top 20 surgeries for highest readmission rates, yet PUL has nearly none. The Blue Cross Blue Shield Association draft analysis has inaccuracies that I will address below. Most importantly, Blue Cross Blue Shield Association draft analysis is conducted in a vacuum without references that are available for other BPH services. The clinical evidence supporting PUL is superior in quality and at least similar in quantity to most Blue Cross Blue Shield Association recommended BPH treatment services. While there can always be criticisms of scientific studies, the key point is to determine whether the evidence is sufficient to understand the treatment effect on net health outcomes. The answer to this is "yes" when it comes to PUL. PUL studies show irrefutably and consistently that symptoms,

No.	Additional Comments
	quality of life, and urinary flow improve. PUL is done with clearly lower morbidity than other currently recommended BPH procedures. Importantly, it has been consistently demonstrated to be the only treatment option that protects a patient from losing sexual function. There is clear dissidence between the Blue Cross Blue Shield Association analysis of clinical evidence and the draft conclusion that the evidence is in any way insufficient to determine utility and effect on net health outcomes. One may ask in this field, "what is net health outcome?" It is not just an AUA Symptom Index improvement, nor an improvement in urinary flow; it is both of these without causing unnecessary harm to the patient (e.g. sexual dysfunction; urinary incontinence; extended recovery; readmissions for bleeding, clot retention, and ER visits due to catheterization, etc.). PUL offers this complete package as well as, or better than, any BPH service that Blue Cross Blue Shield Association currently recommends.
3	Nothing Listed
4	In short- to medium-term studies, PUL shows improvement in patient symptom score. This provides a meaningful alternative to medical management or transurethral resection/ablation of the prostate. The benefit of PUL is that it can be done under minimal sedation, which provides a possibility of a procedure to benefit patients who have failed or cannot tolerate medical therapy but who are at high risk for general anesthesia. In addition, PUL can be performed safely for patients on anticoagulation, and this provides a significant benefit compared to TURP given that the risk of bleeding from TURP on anticoagulation is high, and this provides an alternative with a lower complication risk in that regard. Finally, the PUL sutures can be later removed during TURP, so this therapy does not preclude a TURP in the future if necessary for improved symptom control.

5. Is there any evidence missing from the attached draft review of evidence that demonstrates clinical benefit?

No.	Yes/ No	Citations of Missing Evidence
1	No	
2	Yes	I would like to offer my corrections/edits of the analysis: 1. Sexual Function analyses: there appears to be a misunderstanding of the treatment goal of this therapy. PUL is not designed to improve sexual function; it is the only BPH treatment to ever show that it does not cause sexual dysfunction. Mean MSHQ scores stay stable or improve, which is good, but the most important sexual function data are that there have been no (0) accounts of induced sexual dysfunction with PUL, compared to 65% to 90% for standard surgery and 8%-16% for heat ablation. This is a very important consideration from a defensive medicine perspective. By not allowing access to PUL, a provider and/or insurer is causing a patient to undergo an unnecessary risk of losing part or all of his sexual function and lifestyle. No other option can preserve sexual function as reliably as PUL. 2. BPH6 ejaculatory dysfunction (EjD) endpoint was not a mean score, but instead how many men completely lost the ability to ejaculate: 40% TURP vs 0% PUL. Definitively favorable result among PUL patients. Blue Cross Blue Shield states that PUL was non-inferior in the BPH6 endpoint. You are correct. It was actually proven SUPERIOR. Blue Cross Blue Shield states that the evidence do not support the conclusion despite the published fact that the statistical analysis, including and accommodating for the anticipated loss of TURP randomized subjects, does in fact support that conclusion. Blue Cross Blue Shield gives no scientific reason why they disagree with the science. 3. The analysis states of the LIFT study that there were 9 serious adverse events (SAE) in the PUL arm versus 1 in the sham control and then 16 more in the PUL arm. This is a very misleading statement and should be corrected. Of relevance is simply the number of related SAE. There was 1 related SAE in the first 3 months (an overnight stay related to clot retention for a PUL patient, which outside of a clinical study would not characterized as serious, and certainly is not uncommon for other BPH treatment options) and one thereafter (removal of a bladder stone that formed from smaller bladder calcification confirmed as existing prior to PUL). Please read the text of the Roehrborn article to further understand the adverse event table.

No.	Yes/ No	Citations of Missing Evidence
		4. Crossover Study: the analysis states that there was no difference in improvement in Qmax after PUL versus after sham. This represents a misunderstanding. After sham, Qmax improved 2ml/s. After PUL, it improved another 2ml/s, showing a cumulative increase of 4ml/s over baseline. A Qmax change of 4ml/s is exactly what was seen in the randomized study for PUL. 5. LIFT Study: The analysis states that the 5-year report showed a difference between ITT and per protocol results. This is false. Also, the analysis states that the average AUASI improvements were -7.85 ITT versus -10.61 PP. This too, is false. The publication shows the following: -7.85 ITT versus -7.56 PP, and as stated in the Discussion section, there was no statistical difference, which effectively shows the small loss to follow up had no effect on outcomes analysis. 6. LIFT Study: "87 analyzed in CONSORT vs 104 in text." Please remove this statement or clarify. Without explanation, the statement implies an error, rather than a misunderstanding. As explained in the article text, 104 of 140 subjects were available for follow up and there was a detailed explanation of each of the 36 subjects with missing data. Of the 104, 87 had no surgical retreatment or protocol deviation. 7. LIFT Study Summary: "high loss to follow up" statement is not warranted when compared to currently covered BPH services. Over 80% of living subjects had available data at 5 years. This is truly unparalleled in the field of BPH studies. Perhaps the Blue Cross Blue Shield Association team is comparing this study to pharmaceutical studies from other disease states, etc. In the context of whether PUL has been studied at least as well, if not better, than currently covered services in BPH, the answer is a definitive "yes". 8. Section Summary: Table 4. I fail to see why treating men who are washed out of medication is "not standard or optimal" when this is true of every other BPH study conducted that supports any covered BPH procedure. Of course, we would not wash patients out of medication to treat them with PUL, but to not do so in a clinical study would create tremendous bias in the data. This is well understood by AUA, NIH, CMS and FDA. "Unclear history of BPH treatments" - no patient had undergone a prior BPH procedure in the studies. "Unclear intended use" - there is no published clinical study of Blue Cross Blue Shield currently covered BPH services that distinguish between treating men after or before medication usage. As such, it is irrelevant that this is also true of the bibliography supporting PUL. 9. Table 5: "high loss to follow up/exclusions; only LOCF ITT analysis provided". This statement is again not reflective of the body of evidence supporting Blue Cross Blue Shield covered services. The fact that LIFT included 74% subjects at 5 years and analyzed both PP and ITT is the very state of the art in BPH - it does not exist in most other currently covered services. 10. Summary of Evidence: please correct these paragraphs with the above-mentioned points. 11. Practice Guidelines and Position Statements: • AUA - there is no mention that a publicly available position statement exists where AUA states that US patients should have access to PUL, a proven BPH treatment. Please include this. • EAU - The European Association of Urology publishes BPH guidelines semi-annually. They rate the PUL clinical evidence as Level 1A on the Oxford score, which is the highest possible rating. • Medicare National Coverage - please include / mention that no BPH treatment has ever been reviewed for national coverage determination.
3	No	
4	No	

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41. Foster HE, Barry MJ, Dahm P, et al. Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA GUIDELINE. 2019. https://www.auanet.org/guidelines/benign-prostatic-hyperplasia-(bph)-guideline. Accessed June 24, 2019.
42. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 7.01.151 (August 2019).

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Documentation of no urinary retention, urinary tract infection, or recent prostatitis (within the past year)
  - Past medical and/or surgical treatment(s) and response(s) (within the past year)
- Laboratory report(s), including prostate gland volume and prostate-specific antigen levels
- Radiology report(s)

Post Service

- Results/reports of tests performed
- Procedure report

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

MN/IE

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

Type	Code	Description
CPT®	52441	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant
	52442	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable

Type	Code	Description
		transprostatic implant (List separately in addition to code for primary procedure)
HCPCS	C9739	Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants
	C9740	Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants
ICD-10 Procedure	0T7D8DZ	Dilation of Urethra with Intraluminal Device, Via Natural or Artificial Opening Endoscopic
	0TUD8JZ	Supplement Urethra with Synthetic Substitute, Via Natural or Artificial Opening Endoscopic

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
04/30/2015	Custom policy	Medical Policy Committee
10/01/2016	BCBSA Medical Policy adoption – changed from Custom policy BSC7.07 to BCBSA-based policy 7.01.151 Policy revision without position change	Medical Policy Committee
10/01/2017	Policy revision without position change	Medical Policy Committee
10/01/2018	Policy revision with position change	Medical Policy Committee
12/01/2019	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.