MEDICAL POLICY

Prostate: Prostatic Urethral Lift

Effective Date: 1/1/2020

Technology Assessment Committee Approved Date: 1/14; 2/15; 2/16

Medical Policy Committee Approved Date: 3/17; 5/17; 9/17; 11/18; 12/19

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

I. The prostatic urethral lift (PUL) procedure (i.e. UroLift®) utilizing a maximum of 7 implants may be considered medically necessary and covered for the treatment of symptomatic benign prostatic hyperplasia (BPH) when all of the following criteria (A.-D.) are met:

   A. Patient is age 50 or older; and
   B. Patient has moderate-to-severe chronic lower urinary tract symptoms (defined as an American Urologic Association or International Prostate Symptom Score ≥8); and
   C. Pharmacologic BPH treatment has been unsuccessful or intolerable; and
   D. Patient meets all of the following indications for the PUL procedure:
      1. Has a prostate volume less than 80cc; and
      2. Does not have an obstructive or protruding median lobe of the prostate; and
      3. Does not have an active urinary tract infection (UTI).

II. The prostatic urethral lift is considered investigational and not covered when criterion I. above is not met.
CPT/HCPCS CODES

<table>
<thead>
<tr>
<th>All Lines of Business</th>
<th>CPT/HCPCS Code</th>
<th>Description</th>
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<tr>
<td>Prior Authorization Required effective 7/1/17</td>
<td>52441</td>
<td>Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant</td>
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<tr>
<td></td>
<td>52442</td>
<td>Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)</td>
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<tr>
<td>Prior Authorization Required effective 9/1/17</td>
<td>C9739</td>
<td>Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants</td>
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<td></td>
<td>C9740</td>
<td>Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants</td>
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DESCRIPTION

Benign Prostatic Hyperplasia (BPH)

BPH is an enlargement of the prostate gland. The prostate gland sits below the bladder and encircles the urethra (the tube that carries urine out of the body). The prostate naturally grows with age, and as it grows it can begin to compress the urethra and because of this, BPH is very common in aging men. Approximately 50% of all men age 51 to 60 have BPH, and approximately 90% of men over the age of 80 have BPH. Many men with BPH do not have symptoms. Men that do have symptoms usually experience frequent urination, a weak urine stream, and/or leaking urine. These BPH symptoms are commonly referred to as lower urinary tract symptoms (LUTS). The treatment for LUTS usually depends on the severity of symptoms. Men with mild BPH may start with life style changes; while men with moderate-to-severe BPH typically require treatment with medications and possibly surgery.

Treatment of BPH

Pharmacologic Therapy

There are two types of medicines used to treat BPH: alpha blockers and alpha-reductase inhibitors. Typically, men who start taking BPH medicine will need to take it forever unless surgical treatment is undertaken. Alpha blockers may be used to treat LUTS related to BPH by relaxing the muscles of the prostate and bladder neck; thus reducing the pressure on the urethra and more urine flow. Alpha blockers begin to work quickly and are usually recommended as the first-line of treatment for mild-to-moderate BPH symptoms. Alpha-reductase inhibitors stop the prostrate from growing and can even cause it to shrink. This type of medication is recommended for men with larger prostates and can take up to six months for symptom improvement. Common side effects of both BPH medicines include dizziness, loss of libido, and sexual dysfunction. These side effects and the need for life-long BPH medication compliance, lead 30% of men to discontinue their BPH medicine after the first year.
Transurethral Resection of the Prostate (TURP)

TURP is a surgical treatment for BPH that involves the removal of obstructing tissue from the prostate. In the United States, about 150,000 men have TURPs each year. The procedure is typically performed under general or spinal anesthesia and requires a 24-48 hour postoperative catheterization observation period. The average recovery time after the TURP procedure is anywhere from 4 to 12 weeks, and patients may also experience a postoperative worsening of LUTS for 4 to 6 weeks. On average, TURP results in a 14.9 International Prostate Symptom Score (IPSS) improvement; therefore making it the gold standard surgical intervention for treatment of BPH. However, due to the invasive nature of the TURP procedure it is associated with more serious and possibly chronic complications including loss of ejaculatory function (65%), erectile dysfunction (10%), incontinence (3%), excessive bleeding requiring transfusion (2.9%), transurethral resection syndrome (1.4%), and stricture formation (7%). Although the TURP procedure significantly improves LUTS, these potential adverse side effects could considerably impact a patient’s quality of life; therefore, new surgical techniques have been proposed as less invasive alternatives to TURP.

Prostatic Urethral Lift (PUL) (UroLift®)

The PUL procedure (i.e. UroLift®) is a surgical treatment for BPH that involves the placement of small mechanical sutures which hold the enlarged prostate tissue out of the way so it no longer blocks the urethra. This is done by placing small, non-absorbable suture implants with a metallic anchor into the lateral (side) lobes of the prostate. These sutures mechanically separate the lobes in order to help relieve pressure and increase the opening of the urethra. Four to five implants are usually inserted, but this number varies with the size and shape of the prostate. Since the PUL procedure does not remove any obstructing prostate tissue and typically only requires local anesthesia, it is less invasive than other surgical BPH treatments. PUL is typically performed in the doctor’s office by an appropriately trained urologist.

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of prostatic urethral lift procedure (PUL) (UroLift®) as a treatment for lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). Below is a summary of the available evidence identified through November 14, 2018.

Systematic Reviews

- In 2016, the ECRI Institute published a health technology assessment of the UroLift® procedure for treating BPH symptoms. The authors systematically searched for relevant research published between January 2011 and October 2016 and included three systematic reviews and two randomized controlled trials (RCTs). The evidence suggested that the UroLift® procedure was well-tolerated and works as intended for treating BPH symptoms in most patients for up to three years. The ECRI authors also identified the potential benefit of UroLift® for preserving sexual function and quality of recovery compared to TURP. However, 10.7% of UroLift® treated patients experienced treatment failure that required surgical re-intervention. The assessment also noted that 363
UroLift®-related complications had occurred across 7 studies, but more than 95% of these complications resolved without medical intervention. Ultimately, the ECRI assessment acknowledged the promising technology of the UroLift® procedure, but concluded that future RCTs are needed to confirm the results.

• In 2016, Hayes published a systematic review which included 5 clinical studies (2 RCTs, 2 prospective cohort studies, and 1 retrospective database review) that evaluated the efficacy and safety of the PUL procedure using the UroLift® system for treatment of LUTS related to BPH.10 The systematic review suggested that PUL was superior to TURP in regards to improvement of the International Prostate Symptom Score (IPSS) and Benign Prostatic Hyperplasia Impact Index (BPHII), early relief of BPH symptoms, and preserving sexual function. However, TURP was reported as superior to UroLift® at improving post-void residual volume (PVR) and peak urinary flow rate (Qmax). The included studies reported minor adverse events, such as dysuria (pain when urinating), hematuria (blood in urine), pelvic pain, and urinary tract infections (UTIs). Hayes acknowledged that the UroLift® device does not appear to compromise sexual function and that the adoption of this device, in appropriately selected patients, may reduce the utilization of inpatient hospital services that are required for more invasive procedures; both of which were reported as significant advantages of this device compared to TURP. Hayes considered the studies included in the review to be of low-quality due to small sample sizes, lack of comparison groups (only 1 RCT was a head-to-head comparison), limited follow-up time, and losses to follow-up. Hayes gave an overall C rating for use of the UroLift® System as a treatment of LUTS caused by BPH. This rating was based on the low-quality body of evidence noted above and the, “substantial uncertainty that remains due to the dearth of comparative studies and limited long-term evidence regarding the durability and safety of this device.”10

• In November 2017, Hayes published a “Health Technology Brief” in which no change to the C-rating was made. The review notes that while four to five implants are typically inserted, this number “varies with the size and shape of the prostate” and that “some patients may require more than 6 Urolift implants to be placed during the procedure.” The need for additional implants is assessed via cystoscopic evaluation following each implant.30

• In 2016, Jones et al. conducted a good-quality systematic review to identify, appraise, and synthesize the existing evidence for the UroLift® device to treat LUTS secondary to BPH.21 Two independent reviewers conducted a systematic literature search following pre-defined inclusion/exclusion and quality criteria. Ultimately 7 studies (2 RCTs, 1 crossover trial, and 4 cohort studies) were selected for inclusion, with a total of n=440 patients included. The authors divided the outcome measures of the selected studies into two categories: objective (measurable) outcomes and subjective (opinion based) outcomes. The objective outcome measures included prostate-specific antigen (PSA), post-void residual (PVR) volume, and maximum urinary flow rate (Qmax). The subjective outcome measures included in the systematic review were the International Prostate Symptom Score (IPSS), Quality of Life (QoL), International Index of Erectile Function (IIEF), and Sexual Health Inventory for Men (SHIM).

The UroLift® procedure exhibited improvements in both objective and subjective outcome measures; however, the most significant improvements were in the subjective measures. Unlike TURP, the UroLift® did not demonstrate significant, long-term improvements in PVR and Qmax. The authors suggested that studies with longer follow-up periods were needed to confirm its durability and long-term efficacy. The review also evaluated the UroLift® safety profile in the selected studies.
Authors reported the UroLift had favorable advantage over TURP in the ability to preserve sexual function. The authors also recognized that careful patient selection was vital when choosing to perform UroLift, given all the explicit indications for the procedure, and that the efficacy and safety had yet to be proven among men with more complicated health problems. There were several strengths of this systematic review, including the selection of high quality studies which were published within the last 5 years and the systematic approach taken for selecting literature and extracting data. Limitations of this systematic review were due to the limited number of quality studies on the UroLift® procedure and the inability to conduct a meta-analysis because the selected studies varied in type and quality. Ultimately, the authors concluded that the UroLift® procedure, “may not be an end-of-the-line intervention but rather, an intermediate, minimally invasive option for a specific population of men who wish to preserve sexual function as a key priority in their treatment.”

Randomized Controlled Trials (RCTs)

- The L.I.F.T. study (Luminal Improvement Following Prostatic Tissue Approximation for the Treatment of LUTS secondary to BPH) was a prospective, randomized, controlled, blinded study conducted across 19 centers in the United States, Canada, and Australia. Participants were eligible for inclusion under the following criteria:

  1. >50 years old
  2. IPSS ≥13
  3. Peak flow (Qmax) ≤12 mL/s
  4. Prostate volume 30-80cc
  5. Absence of obstructive median lobe
  6. Absence of active UTI

A total of 206 participants were enrolled and randomized 2:1 into the treatment (PUL) and sham groups (PUL=140, sham=66). Blinding was done by placement of a surgical screen to block the patient’s view and the outcome assessment was completed by someone who was not involved in the original procedure. The sham procedure involved rigid cystoscopy (a procedure to check for any problems in the bladder) with simulated active treatment sounds. PUL participants received anywhere from 2-11 implants. The outcomes of interest were IPSS, QoL, BPH Impact Index, Qmax, sexual function, and adverse events. After the 3 month follow-up, the sham patients were unblinded and offered enrollment into a crossover study where they would receive PUL treatment and be followed for 24 months (Rukstalis et al. study described below).

The L.I.F.T. RCT is now reporting results on effectiveness, safety, and durability from their 5 year follow-up. The effectiveness of the PUL procedure in regards to IPSS, QoL, BPH Impact Index, Qmax has been sustained through 5 years. The most significant adverse event reported was encrustation of the implant(s) caused by urine exposure when placed too close to the bladder. Of the 642 implants placed during the L.I.F.T. study, 14 implants (2%) in 10 subjects were encrusted and had to be removed. Other reported adverse events were mild-to-moderate and resolved within 2-4 weeks without treatment. In regards to durability of the UroLift® procedure, 13.6% of the 140 originally enrolled subjects required surgical retreatment. Conversely, additional LUTS treatment after TURP is estimated to be about 6% at 2 years and 8% at 5 years. Sexual function was also evaluated in the L.I.F.T. patients. There were no reports of sexual dysfunction (erectile dysfunction...
and ejaculatory dysfunction) following the PUL procedure. Also, all patients were able to undergo
the procedure under local anesthesia in the urologist’s office. The authors attempted to standardize
the number of required implants by evaluating prostate size and number of implants placed, but no
correlation was found.

The methodological strengths of this study included recruitment from 19 different health centers
across 3 countries, a large sample size based on a power calculation, randomized design, blinding,
and comparison to a sham procedure. Analysis was also conducted using the intention-to-treat
methodology and patients that experienced protocol deviations or had other prostate-related
treatments were censored out of the analysis. Limitations of the L.I.F.T. RCT include the subjective
nature of 4 of the 6 outcomes of interest, short follow-up of the sham group (3 months), significant
losses to follow-up by year 4, and no comparison to a standard of care surgical BPH treatment (i.e.
TURP).

• Gratzke et al. conducted a prospective, multi-center, randomized study to compare PUL to TURP for
the treatment of LUTS secondary to BPH. Currently, this is the only head-to-head comparison of
PUL using the UroLift® device with the gold standard TURP procedure. Subject eligibility was based
on the following criteria:

1. ≥50 years old
2. IPSS > 12
3. Q\text{max} ≤ 15 mL/s
4. Prostate volume ≤ 60 cc per ultrasound.

A total of n=80 participants were recruited from 10 different European health centers, randomized
1:1, and followed for 2 years. The primary study endpoint, the BPH6 questionnaire, was specifically
designed for this RCT. The BPH6 is a composite of the following 6 other validated questionnaires
which assesses overall health:

1. International Prostate Symptom Score (IPSS)
2. Sexual Health Inventory for Men (SHIM)
3. Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD)
4. Incontinence Severity Index
5. Quality of Recovery Visual Analog Score
6. Clavien-Dindo classification of adverse events (AEs)

Secondary endpoints were measures of patient satisfaction, quality of life (QoL), BPH Impact Index,
peak flow rate (Q\text{max}), and sleep disturbances.

Significant improvements were seen in both groups; however, TURP was superior to PUL for
improvements in IPSS and Q\text{max}, while PUL was superior to TURP for QoL, quality of recovery, and
postoperative sexual function. At the 2 year follow-up, 100% of PUL patients had preserved sexual
function while 34% of TURP patients reported ejaculatory dysfunction. TURP patients also
experienced a statistically significant worsening of continence function at the 2 week and 3 month
follow-up (> 1 point change from baseline for the incontinence severity index (ISI) score) while the
PUL patients maintained baseline continence throughout the 2 year follow-up. In regards to 2 year
durability of PUL versus TURP, 6 PUL patients (13.6%) and 2 TURP patients (5.7%) required secondary treatment for return of LUTS during the follow-up period.

Strengths of this RCT included its randomized, controlled design and recruitment from 10 different health centers across Europe. Limitations are due to the small sample size, short follow-up period, and lack of blinding. A significant limitation of this RCT was the use of the BPH6 questionnaire as the primary endpoint. Although the authors stated the questionnaire is based on validated questionnaires, the BPH6 itself has yet to be validated. Using this questionnaire as the primary endpoint of the RCT creates a significant amount of doubt as to the reliability and validity of these results.

Nonrandomized Studies

- Rukstalis et al. evaluated the 2 year effectiveness and durability of PUL in a cross over study of the L.I.F.T. RCT sham patients. Participants were eligible for inclusion under the criteria as the original L.I.F.T. RCT.

A total of 51 patients were enrolled in the crossover study, underwent the PUL procedure, and were followed-up through 24 months. The selected outcomes of interest were IPSS, $Q_{\text{max}}$, QoL, and BPH Impact Index. The PUL procedure was efficacious for all outcomes through 24 months. Also, sexual function was preserved in all patients with no reported incidences of erectile or ejaculatory dysfunction. The reported adverse events were mild-to-moderate and typically resolved within 2 weeks. Of the 241 devices implanted in the cross over patients, 10 devices (4%) were found to have encrustation due to improper placement and required removal. Also of note, 4 patients (8%) progressed to TURP and 1 patient (2%) required additional PUL implants. Methodological strengths of this study included recruitment out of 19 health centers across 3 countries and the randomized design (from the L.I.F.T. RCT). Limitations included the small sample size and short follow-up period. There were 15 losses to follow-up and no comparison to the gold standard surgical BPH treatment. Also, bias of the results is probable because 3 of the 4 outcome measures were subjective.

- Sievert et al. (2018) evaluated the 2 year effectiveness of Urolift among 86 patients electing the procedure instead of transurethral resection of the prostate (TURP).

At 2 years, 86% (n=74) of patients reported statistically significant improvement in symptoms, flow and quality of life. Some patients, 12.8% (n=11), reported persistence of LUTS or remaining PVR, only two of whom elected more implants, one of whom improved while the other did not. Adverse effects were minimal. Limitations include the relatively short follow-up period (2 years); very poor response rate at follow up (47%) and non-randomized study design. Inclusion criteria were also broader than most North American studies, with no exclusions made on the basis of high post-void residual volume (PVR), prostate size, retention history or LUTS oral therapy.

Walsh (2017) gave an overview of advanced surgical techniques for PUL surgery. Walsh noted that, “while four implants are sufficient for many prostates, there are particular anatomical variations that require additional implants. Long prostatic urethras may require three implants along the length of each lateral lobe. Patients with a high bladder neck, a modest non-obstructing median lobe or protruding anterior tissue may benefit from supplemental implant(s) near the bladder neck.”
In a narrative review of five recent PUL clinical studies (n=44-137), Roehrborn (2016), lead investigator of the LIFT study, noted that the average number of implants patients receive ranges from 3.7 to 4.9.33

**CLINICAL PRACTICE GUIDELINES**

**National Institute for Health and Care Excellence (NICE)**

The 2016 NICE guidelines recommend the use of the UroLift® system for treating lower urinary tract symptoms caused by benign prostatic hyperplasia. They recommend the UroLift® system be, “considered an alternative to current surgical procedures for use in a day-case setting in men with lower urinary tract symptoms of benign prostatic hyperplasia who are aged 50 years and older and who have a prostate less than 100 mL without an obstructing middle lobe.”12 The NICE committee also conducted a cost analysis for the UroLift® procedure compared to the gold standard TURP procedure. They concluded that using the UroLift® in a day-surgery unit resulted in a cost savings of around $358-$199 per patient.

**American Urological Association (AUA)**

The AUA does not address the UroLift® procedure in their most recent guideline for the diagnosis and treatment of benign prostatic hyperplasia (the guideline was released in 2010 and UroLift® received FDA approval in 2013).14 However, the AUA issued a letter of communications with medical directors in January 2015 stating that the, “UroLift® prostatic procedure should not be considered investigational but an appropriate therapeutic tool used by urologists.”13

**Sexual Medicine Society of North America (SMSNA)**

The SMSNA released a position statement in April of 2017 indicating their support for the UroLift® procedure as a treatment of LUTS secondary to BPH. Although this is not an evidence-based clinical practice guideline, they recognize UroLift® as a treatment option for men with symptomatic BPH due to the available evidence supporting its, “favorable sexual side effect profile over alternative therapies.”15

**Health Evidence Review Commission (HERC) Oregon**

The 2015, HERC coverage guidance for surgical alternatives to TURP did not recommend the use of prostatic urethral lift as a for treatment of LUTS.16 However, this guidance was approved in March of 2015 and the evidence review did not include some of the more recent pivotal studies (e.g. the Gratzke et al. head-to-head RCT and the 4 year L.I.F.T. RCT results).

**CENTERS FOR MEDICARE & MEDICAID**

As of November 2018, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses prostatic urethral lift as a treatment of BPH.

**SUMMARY**
Although current evidence does not support the durability or efficacy of PUL compared to TURP, PUL appears to have significant advantages over TURP due to the less invasive and more convenient nature of the procedure. One of the most notable advantages of the PUL procedure is its ability to significantly preserve sexual and continence function compared to TURP. However, due to the limited number of PUL versus TURP RCTs it should not be seen as a replacement for TURP, but rather as an intermediate, minimally invasive option which may prolong the time to a more invasive surgical treatment. While patients typically require 4 implants, patient anatomy varies and some individuals may require additional implants to durably ensure prostatic deobstruction. Long-term, high quality prospective studies are needed to confirm the long-term efficacy of the PUL procedure as a treatment for LUTS related to BPH.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

REFERENCES


