

2.01.49 Transurethral Water Vapor Thermal Therapy for Benign Prostatic Hyperplasia			
Original Policy Date:		Effective Date:	March 1, 2020
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Policy Statement

Transurethral water vapor thermal therapy is considered **investigational** as a treatment of benign prostatic hyperplasia.

Policy Guidelines

Effective January 1, 2019 a new CPT code describes transurethral water vapor thermal therapy:

- **53854:** Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy

Effective January 1, 2020 a new Pass Through code was created as a result of an application by Procept for the AquaBeam® System. Per the manufacturer, it is intended for the resection and removal of prostate tissue in males suffering from lower urinary tract symptoms due to benign prostatic hyperplasia.

- **C2596:** Probe, image guided, robotic, waterjet ablation

Effective January 1, 2020 there is a new CPT for ultrasound guided transurethral ablation of prostate tissue for treating prostate cancer using thermotherapy with water vapor generated by high energy direct current.

- **0582T:** Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance

Description

Transurethral water vapor thermal therapy is a minimally invasive alternative to transurethral resection of the prostate (TURP). Transurethral water vapor thermal therapy is a process by which water vapor is created outside of the body and delivered to the prostate with a needle. The procedure uses radiofrequency-generated water vapor (~103°C) thermal energy to ablate prostate tissue. The treatment is repeated in multiple locations within the prostate. During the procedure, saline irrigation cools and protects the surface of the urethra. The heat from the vapor disrupts cell membranes in the prostate, which leads to cell death and necrosis.

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

In September 2016, the Rezum System™ (NxThera, Inc) was cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process (K150786). The Food and Drug Administration determined that this device was substantially equivalent to existing devices (Medtronic Prostate devices). Rezum™ is intended to relieve symptoms, obstructions, and reduce prostate tissue associated with benign prostatic hyperplasia. It is indicated for men > 50 years of age with a prostate volume >30cm³ and <80cm³. The Rezum System™ is also indicated for the treatment of prostate with hyperplasia of the central zone and/or a median lobe.

Rationale

Background

Benign prostatic hyperplasia (BPH) is a common condition in older men, affecting to some degree 40% of men in their 50s, 70% of those between ages 60 and 69, and almost 80% of those ages 70 and older.¹ BPH is a histologic diagnosis defined as an increase in the total number of stromal and glandular epithelial cells within the transition zone of the prostate gland. In some men, BPH results in prostate enlargement which can, in turn, lead to benign prostate obstruction and bladder outlet obstruction, which are often associated with lower urinary tract symptoms including urinary frequency, urgency, irregular flow, weak stream, straining, and waking up at night to urinate. Lower urinary tract symptoms is the most commonly presenting urological complaint and can have a significant impact on the quality of life.¹

BPH does not necessarily require treatment. The decision on whether to treat BPH is based on an assessment of the impact of symptoms on quality of life along with the potential side effects of treatment. Options for medical treatment include alpha-1-adrenergic antagonists, 5-alpha-reductase inhibitors, anticholinergic agents, and phosphodiesterase-5 inhibitors. Medications may be used as monotherapy or in combination.²

Patients with persistent symptoms despite medical treatment may be considered for surgical treatment. The traditional standard treatment for BPH is transurethral resection of the prostate.

Transurethral water vapor thermal therapy has been investigated as a minimally invasive alternative to transurethral resection of the prostate. The procedure uses radiofrequency-generated water vapor (~103°C) thermal energy to ablate prostate tissue.³

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.

Clinical Context and Therapy Purpose

The purpose of transurethral water vapor thermal therapy in patients who have benign prostatic hyperplasia (BPH) is to provide a treatment option that is an alternative to or an improvement on existing therapies such as transurethral resection of the prostate (TURP).

The question addressed in this evidence review is: Does transurethral water vapor thermal therapy improve the net health outcome in patients with BPH?

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

Patients

The relevant population of interest are men with BPH.

Symptoms include urinary frequency, urgency, irregular flow, weak stream, straining and getting up at night to urinate.

Interventions

The therapy being considered is transurethral water vapor thermal therapy.

This procedure involves the transurethral injection of steam into the prostate. Once injected, the steam condenses to water, imparting convective energy to the tissue, causing cell death and damage. The technology uses radiofrequency to boil the water to create the steam that is injected but does not impart radiofrequency directly to the prostate tissue. Patients typically require catheterization for at least one week due to post-procedure sloughing of prostatic tissue. The procedure is typically performed in an outpatient setting. Medical management of pain and anxiety may also be required.

Comparators

The following practices and therapies are currently being used to make decisions about transurethral water vapor thermal therapy:

- Conservative treatment, including watchful waiting and lifestyle modifications
- Pharmacotherapy
- TURP
- Other minimally invasive procedures

Outcomes

The general outcomes of interest are symptoms, functional outcomes, QOL, retreatment rates, and treatment-related morbidity.

The International Prostate Symptom Score (IPSS) is used to assess the severity of BPH symptoms. The first seven questions address urinary frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying and urgency each on a scale of 0 to 5. The total score, summed across the 7 items measured, ranges from 0 (no symptoms) to 35 (most severe symptoms). A decrease in score indicates improvement.

QOL is assessed with various scales including the IPSS-QOL.

Erectile and ejaculatory function is assessed in sexually active men only. Scales include the International Index of Erectile Function and the Male Sexual Health Questionnaire. Both short-term (up to 12 months) and long-term (12 months and longer) outcomes should be assessed. Treatment-related morbidity can also be assessed in the immediate post-procedure period. In an RCT, 69% of patients received oral sedation only, 21% received a prostate block, and 10% received intravenous sedation.

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

Transurethral water vapor thermal therapy has been evaluated in one RCT conducted in 197 men (Table 1). Three-month results were reported in McVary et al (2015).⁴

The trial also had an uncontrolled, open-label crossover phase. After unblinding at three months, control subjects who elected to proceed were requalified for the crossover study. A total of 97 patients were followed through 3 years and 90 patients through 4 years. Three-year results were reported in McVary et al (2018)³ and 4-year results in McVary et al (2019).⁵ These results are shown in Table 1.

Table 1. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
McVary et al. (2015, ⁴ 2018 ³), 2019 ⁵ , NCT01912339	US	15	2013-2016	Men with moderate to severe symptomatic BPH, at least 50 years of age (61% were under age 65) with IPSS ≥13, a prostate volume of 30 cc to 80 cc, maximum urinary flow rate (Qmax) of ≤15 mL/s, and a measured postvoid residual (PVR) urine <250 mL. Exclusion criteria included a prostate specific antigen >2.5 ng/mL with a free prostate specific antigen <25% (unless prostate cancer was ruled out by biopsy) and an active urinary tract infection.	n=136 Transurethral water vapor thermal therapy (Rezüm)	n=61 Sham procedure with rigid cystoscopy and activation of the system generator outside the subject's body to mimic the sound of the active procedure.

BPH: benign prostatic hyperplasia; IPSS: International Prostate Symptom Score; RCT: randomized controlled trial.

Results of the RCT are shown in Table 2. The primary outcome was the difference in the change from baseline between the treatment and control arms at three months post-treatment. The secondary outcome was the percentage of responders at three months. Response was defined as a 30% or greater improvement (reduction) in the IPSS at 3 months compared to baseline. The Rezüm group showed an 11.2-point decrease in IPSS, vs a 4.3-point decrease in the sham group ($p<0.001$). There were more responders (defined as 30% or more improvement in the IPSS) in the Rezüm group. Notably, more than half of the patients in the control group were classified as responders at three months. There were significant differences in other measures of lower urinary tract symptoms and QOL.

One hundred thirty of the 197 participants (70.0%) reported being sexually active at baseline and were assessed for erectile function. There were no significant changes in erectile or ejaculatory function at follow-up and no differences between groups. That is, the treatment was not associated with adverse effects on erectile or ejaculatory function.

Two patients in the Rezum group experienced three serious procedure-related adverse events: one patient had de novo extended urinary retention and another had nausea and vomiting due to alprazolam and was hospitalized overnight for observation.

Table 2. Summary of Key RCT Results

Study	IPSS change from baseline	Responders (30% improvement in IPSS)	IPSS QoL	Qmax (mL/s)	BPHII	IIEF-EF	MSH Q-EjD function	MSH Q-EjD both	Serious AEs
McVary et al, (2015) ⁴									
N analyzed	197	197	197	194	195	130	130	130	197
Rezum	-11.2 (7.6)	106/136 (77.9%)	-2.1 (1.6)	6.2 (7.1)	-3.4 (3.5)	0.1 (7.4)	0.3 (4.3)	-0.4 (1.9)	66/136 (48.5%)
Sham	-4.3 (6.9)	21/61 (59.5%)	-0.9 (1.5)	0.5 (4.2)	-1.5 (3.0)	-1.5 (3.0)	-0.2 (3.2)	-0.2 (1.9)	4/61 (6.6%)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0003	0.0003	0.443	0.623	NR

AE: adverse events; BPH: benign prostatic hyperplasia Impact Index; IPSS: International Prostate Symptom Score; MSHQ-ED Male Sexual Health Questionnaire-Erectile Dysfunction; IIEF: International Index of Erectile Function; NR: not reported; Qmax: peak urinary flow; RCT: randomized controlled trial.

The trial also had an uncontrolled, open-label crossover phase, reported in McVary et al (2018) and McVary et al (2019). After unblinding at three months, control subjects who elected to proceed were requalified for the crossover study. A total of 97 patients were followed through 36 months. These results are shown in Table 3. Urinary symptoms and QOL remained significantly improved from baseline up to four years.

The surgical retreatment rate was 4.4 percent over four years.

Table 3. Results of open-label uncontrolled crossover phase (McVary et al [2018]³ and McVary et al (2019)⁵.

Outcome, mean change from baseline (SD)	3 months	6 months	12 months	24 months	36 months	48 months
IPSS						
N	134	129	121	109	97	90
Change	-11.3 (7.6)	-12.2 (7.6)	-11.6 (7.3)	-11.2 (7.3)	-11.0 (7.1)	-10.1 (7.6)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
IPSS QoL						
N	134	129	121	109	97	90
Change	-2.1 (1.6)	-2.3 (1.6)	-2.2 (1.6)	-2.2 (1.5)	-2.2 (1.6)	-2.0 (1.7)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Qmax						
N	125	119	112	99	80	81
Change	6.4 (7.2)	5.7 (6.2)	5.5 (6.4)	4.8 (6.1)	3.5 (4.7)	4.2 (5.7)
p-value						
PVR volume	133	125	118	106	92	89

Outcome, mean change from baseline (SD)	3 months	6 months	12 months	24 months	36 months	48 months
N						
Change	-10.6 (68.3)	-8.4 (75.8)	-3.9 (82.7)	-0.3 (85.3)	-26.4 (63.9)	-9.2 (72.2)
p-value	0.3459	0.3721	0.8943	0.6549	0.0004	
BPHII						
N	143	129	121	109	97	90
Change	-3.4 (3.5)	-4.1 (3.0)	-3.9 (3.3)	-3.8 (3.1)	-3.7 (3.3)	-3.5 (3.4)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
IIEF-EF						
N	90	84	77	71	62	58
Change	0.1 (7.4)	-0.3 (6.4)	-0.3 (7.5)	-1.2 (7.6)	-1.9 (8.2)	-2.5 (8.7)
p-value	0.8927	0.8816	0.8709	0.4080	0.1119	0.03333
MSHQ-EJD Function						
N	90	83	78	70	63	56
change	0.3 (4.3)	0.1 (3.6)	-0.3 (3.5)	-0.5 (4.2)	-1.4 (3.8)	-1.8 (4.4)
p-value	0.5612	0.7451	0.2778	0.3505	0.0033	0.0038
MSHQ-EJD Bother						
N	90	84	79	70	63	56
change	-0.3 (1.9)	-0.4 (1.9)	-0.7 (1.8)	-0.5 (1.7)	-0.5 (1.6)	-0.1 (1.8)
p-value	0.776	0.951	0.0015	0.0129	0.0060	0.6495

SD: standard deviation; N: number analyzed; IPSS: International Prostate Symptom Score; Qmax: peak urinary flow; PVR: postvoid residual urine volume; BPHII: BPH Impact Index IIEF-EF: International Index of Erectile Function; MSHQ-EJD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction.

Notable relevance and study design and conduct limitations of the RCT reported by McVary et al (2015,⁴ 2018,³ 2019⁵) are summarized in Tables 4 and 5. The major limitations were the short follow-up duration in the sham-controlled phase, and lack of blinding, no control group, and high loss to follow-up in the follow-up phase. Additionally, no studies have compared Rezum to medical management, TURP, or other minimally invasive procedures. Because lower urinary tract symptoms in men with BPH may improve spontaneously over time, it is important for future studies to include a longer follow-up period with a control group.

Table 4. Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
McVary et al (2015) ⁴			2 Sham procedure; no comparison to alternative treatments	5 Clinically significant difference on symptoms not prespecified	1, 2 3 months
McVary et al (2018) ³ and McVary et al (2019) ⁵			2 No control group (comparison to baseline only)	5 Clinically significant difference in symptom outcomes not prespecified	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

^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
McVary et al (2015) ⁴ .					3 Small sample size	
McVary et al (2018) ³ . and McVary et al (2019) ⁵ .		1, 2, 3 open label		High loss to follow-up (97/197 [49%] had 3-year data on primary outcome, 90/197 (46%) had 4-year data)	3 Small sample size	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

^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.

Summary of Evidence

For individuals who have BPH who receive transurethral water vapor thermal therapy, the evidence includes one small, short-term sham-controlled RCT with a four-year uncontrolled follow-up phase. The outcomes of interest are symptoms, QOL, and treatment-related morbidity. At three months, lower urinary tract symptoms improved more in the intervention group compared to the sham procedure. No adverse effects on erectile or ejaculatory function were observed, and improvements were sustained through four years of follow-up. This evidence is limited by the small sample size, short-term duration, lack of blinding of longer-term outcomes, and lack of comparison to alternative treatments such as TURP. The evidence is insufficient to determine the effects of the technology on health outcomes.

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.

Practice Guidelines and Position Statements

The American Urological Association (2018) issued clinical practice guidelines on benign prostatic hyperplasia (amended 2019) and made the following recommendations for water vapor thermal therapy⁶:

- Water vapor thermal therapy may be offered to patients with lower urinary tract symptoms attributed to benign prostatic hyperplasia provided prostate volume <80 g; however, patients should be counseled regarding efficacy and retreatment rates. (Conditional Recommendation; Evidence Level: Grade C)
- Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)

The recommendations were based on results of the randomized controlled trial conducted by McVary et al. (2015,⁴ 2018³), and this body of evidence was considered low strength, leading to a conditional recommendation (Grade C).

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

Some currently unpublished trials that might influence this review are listed in Table 6.

Table 6. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT03605745	Minimally Invasive Prostatic Vapor Ablation-Multicenter, Single-Arm Study for the Treatment of BPH in Large Prostates (Rezūm XL)	88	Aug 2019
<i>Unpublished</i>			
NCT02940392	Rezūm First in Man Feasibility Study for the Treatment of BPH with the Rezūm System	15	Jun 2018 (status unknown)
NCT02943070	NxThera Benign Prostatic Hyperplasia Rezūm System Pilot Study	50	Dec 2018 (status unknown)

NCT: National Clinical Trial

References

1. UpToDate. Medical treatment of benign prostatic hyperplasia. 2019. Available at: https://www.uptodate.com/contents/medical-treatment-of-benign-prostatic-hyperplasia?search=benign%20prostatic%20hyperplasia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed May 28, 2019.
2. Westwood, JJ, Geraghty, RR, Jones, PP, Rai, BB, Somani, BB. Rezūm: a new transurethral water vapour therapy for benign prostatic hyperplasia. *Ther Adv Urol*, 2018 Oct 23;10(11). PMID 30344644
3. McVary, KK, Roehrborn, CC. Three-Year Outcomes of the Prospective, Randomized Controlled Rezūm System Study: Convective Radiofrequency Thermal Therapy for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia. *Urology*, 2017 Nov 11;111:1-9. PMID 29122620
4. McVary, KK, Gange, SS, Gittelman, MM, Goldberg, KK, Patel, KK, Shore, NN, Levin, RR, Rousseau, MM, Beahrs, JJ, Kaminetsky, JJ, Cowan, BB, Cantrill, CC, Mynderse, LL, Ulchaker, JJ, Larson, TT, Dixon, CC, Roehrborn, CC. Minimally Invasive Prostate Convective Water Vapor Energy Ablation: A Multicenter, Randomized, Controlled Study for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. *J. Urol.*, 2015 Nov 29;195(5). PMID 26614889

5. McVary, KK, Rogers, TT, Roehrborn, CC. Rezüm Water Vapor Thermal Therapy for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: 4-Year Results From Randomized Controlled Study. *Urology*, 2019 Jan 25;126:171-179. PMID 30677455
6. American Urological Association Benign Prostatic Hyperplasia: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms, 2018 (amended 2019) Available at: [https://www.auanet.org/guidelines/benign-prostatic-hyperplasia-\(bph\)-guideline](https://www.auanet.org/guidelines/benign-prostatic-hyperplasia-(bph)-guideline). Accessed May 28, 2019.
7. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 2.01.49 (June 2019).

Documentation for Clinical Review

- No records required

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.

IE

The following services may be considered investigational.

Type	Code	Description
CPT®	0582T	Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance (Code effective 1/1/2020)
	53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy (Code effective 1/1/2019)
	55899	Unlisted procedure, male genital system
HCPCS	C2596	Probe, image guided, robotic, waterjet ablation (Code effective 1/1/2020)

Policy History

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

Effective Date	Action
08/01/2019	BCBSA Medical Policy adoption
03/01/2020	Coding update

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of

services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

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 at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 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.