Policy Statement

Unilateral or bilateral nerve graft is considered investigational in patients who have had resection of one or both neurovascular bundles as part of a radical prostatectomy.

Policy Guidelines

Coding

There are no specific CPT codes describing sural nerve grafting of the cavernous nerves; the CPT codes describing nerve grafts specifically identify the anatomic site and do not include the cavernous nerves.

The following CPT code may be used to describe the nerve harvest and grafting component of the procedure:

- 64999: Unlisted procedure, nervous system

Alternatively, the following nonspecific CPT code for nerve repair may be used:

- 64910: Nerve repair; with synthetic conduit or vein allograft (e.g., nerve tube), each nerve
- 64911: Nerve repair; with autogenous vein graft (includes harvest of vein graft), each nerve

Description

Nerve grafting at the time of radical prostatectomy, most commonly using the sural nerve, has been proposed to reduce the risk of postoperative erectile dysfunction.

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

A nerve graft with radical prostatectomy is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).
Several nerve cuff products have been cleared for marketing by the FDA through the 510(k) process. FDA product code: J XI. An example of a human tissue nerve graft product, the Avance® nerve graft (AxoGen), is regulated by the FDA under 21 CFR, Part 1271 regulations for Human Cellular and Tissue-based Products (HCT/P).

**Rationale**

**Background**

**Erectile Dysfunction**

Erectile dysfunction is a common problem after radical prostatectomy. In particular, spontaneous erections are usually absent in men whose prostate cancer required bilateral resection of the neurovascular bundles as part of the radical prostatectomy procedure.

**Treatment**

A variety of noninvasive treatments are available, including vacuum constriction devices and intracavernosal injection therapy. However, spontaneous erectile activity is preferred by patients. Studies have reported results from bilateral and unilateral nerve grafts, the latter involving resection of 1 neurovascular bundle.

There has been interest in sural nerve grafting to replace cavernous nerves resection during prostatectomy. The sural nerve is considered expendable and has been extensively used in other nerve grafting procedures, such as brachial plexus and peripheral nerve injuries. As applied to prostatectomy, a portion of the sural nerve is harvested from 1 leg and then anastomosed to the divided ends of the cavernous nerve. Reports also indicate the use of other nerves (e.g., genitofemoral nerve) for grafting.

**Literature Review**

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to 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 a technology, 2 domains are examined: the relevance and the 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 is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials 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 nerve grafting in patients who have radical prostatectomy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does nerve grafting improve the net health outcome in patients who have had radical prostatectomy with resection of neurovascular bundles?
The following PICOs were used to select literature to inform this review.

**Patients**
The relevant population(s) of interest are men who have radical prostatectomy with resection of neurovascular bundles.

**Interventions**
The therapy being considered is nerve grafting in association with radical prostatectomy.

**Comparators**
The relevant comparator is prostatectomy without nerve grafting.

**Outcomes**
The general outcomes of interest are functional outcomes, quality of life, and treatment-related morbidity.

**Nerve Grafting**
One randomized controlled trial evaluating nerve grafting to reduce the risk of erectile dysfunction has been published; findings were reported by Davis et al (2009).\(^1\) The trial included men age 65 years or younger with normal self-reported baseline erectile function selected for a unilateral nerve sparing radical prostatectomy with preservation of 1 neurovascular bundle. All patients had unilateral neurovascular bundle removal, and patients were randomized to receive or not sural nerve grafting after removal. The primary outcome was potency 2 years postsurgery, defined as the ability to have intercourse with or without erectile dysfunction medication. All patients received the same early erectile dysfunction therapy, including medication and mechanical devices. The investigators sought to detect an absolute difference of 20% between groups (graft, 60% potency rate vs no graft, 40% potency rate). A sample of 200 men was originally planned to provide 80% power. However, after 107 men were randomized, a preplanned interim analysis of evaluable patients found similar potency rates between groups. The data monitoring committee stopped the trial based on its estimate of less than a 5% chance that additional recruitment would result in a significant difference between groups. End point data were available for 66 patients. Potency was achieved in 32 (71%) of 45 sural nerve graft patients and 14 (67%) of 21 control patients (p=0.78). Trialists concluded that unilateral sural nerve graft did not result in an absolute improvement of 20% between groups, but that a smaller effect could not be ruled out. A limitation of the trial was that it was unblinded, which, because men knew the procedure they received, could have impacted self-report of potency.

The literature also includes 2 retrospective cohort studies and 3 case series.\(^2\)\(^-\)\(^6\) The cohort studies are described below.

The cohort study by Kung et al (2015) included 38 patients who underwent nerve grafting after radical prostatectomy and a random sample of 53 control patients who had open prostatectomy without nerve grafting.\(^2\) Control patients had unilateral or bilateral nerve sparing prostatectomy or non-nerve sparing prostatectomy. Complete urinary incontinence, no erectile capacity at baseline, and follow-up data less than 12 months were study exclusion criteria. Unilateral nerve grafting (n=29) and unilateral nerve sparing (n=10) patients did not differ significantly between groups (p>0.05) on various outcomes, including urinary continence, erections sufficient for sex, spontaneous erections, and use of erectile dysfunction medications. Bilateral nerve grafting (n=9) and bilateral non-nerve sparing (n=10) patients had similar outcomes (p>0.05). This study lacked randomization and blinding, and subgroup analyses included small numbers of patients.

The second cohort study, published by Namiki et al (2007), included 113 patients: 19 had unilateral nerve sparing plus sural nerve graft, 60 patients had unilateral nerve sparing with no grafting, and 34 patients had bilateral nerve sparing surgery.\(^3\) Function was assessed using validated questionnaires and, at 2 years, no difference in sexual function scores was
found between the unilateral nerve graft and bilateral nerve sparing patients. At 3 years, similar percentages of patients in the unilateral nerve graft (25%) and bilateral nerve sparing (28%) groups considered their sexual function as fair or good. Urinary function returned to baseline continence in the unilateral nerve graft and bilateral nerve sparing groups at 6 months and in the unilateral nerve sparing group at 12 months. Baseline sexual function differed between groups, which could have biased study findings: the nerve grafted and bilateral nerve sparing patients reported higher baseline function than the unilateral nerve sparing group.

Summary of Evidence
For individuals who have radical prostatectomy with resection of neurovascular bundles who receive nerve grafting, the evidence includes a randomized controlled trial, cohort studies, and case series. Relevant outcomes are functional outcomes, quality of life, and treatment-related morbidity. The randomized controlled trial did not find that unilateral nerve grafting was associated with a statistically significant improvement in potency rates at 2 years postsurgery. Cohort studies also did not result in better outcomes with nerve grafting. 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.

In response to requests from Blue Cross Blue Shield Association, input was received from 4 academic medical centers in 2008; no input was received from physician specialty societies. Input from the 4 centers agreed that this procedure is considered investigational.

Practice Guidelines and Position Statements
The National Comprehensive Cancer Network guidelines on the treatment of prostate cancer (v.2.2018) states: “Replacement of resected nerves with nerve grafts has not been shown to be beneficial” for recovery of erectile function after radical prostatectomy.7

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 currently unpublished trial that might influence this review is shown in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01770340</td>
<td>Nerve Grafting With an Allograft During Radical Prostatectomy - Extended Follow-up in a Prospective Randomized Trial</td>
<td>60</td>
<td>Jan 2019 (unknown)</td>
</tr>
</tbody>
</table>

NCT: National Clinical Trial.

References
1. Davis JW, Chang DW, Chevray P, et al. Randomized phase II trial evaluation of erectile function after attempted unilateral cavernous nerve-sparing retropubic radical

**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.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>55840</td>
<td>Prostatectomy, retropubic radical, with or without nerve sparing</td>
</tr>
<tr>
<td>CPT®</td>
<td>55842</td>
<td>Prostatectomy, retropubic radical, with or without nerve sparing; with lymph node biopsy(s) (limited pelvic lymphadenectomy)</td>
</tr>
<tr>
<td>CPT®</td>
<td>55845</td>
<td>Prostatectomy, retropubic radical, with or without nerve sparing; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes</td>
</tr>
<tr>
<td></td>
<td>64910</td>
<td>Nerve repair; with synthetic conduit or vein allograft (e.g., nerve tube), each nerve</td>
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<td>Nerve repair; with autogenous vein graft (includes harvest of vein graft), each nerve</td>
</tr>
<tr>
<td></td>
<td>64912</td>
<td>Nerve repair; with nerve allograft, each nerve, first strand (cable)</td>
</tr>
<tr>
<td></td>
<td>64913</td>
<td>Nerve repair; with nerve allograft, each additional strand (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
</tr>
</tbody>
</table>
Nerve Graft with Radical Prostatectomy

### 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.