



Medical Coverage Policy

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Male Sexual Dysfunction Treatment: Non-pharmacologic

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Related Coverage Resources

[Collagenase clostridium histolyticum](#)
[Oral Phosphodiesterase-5 \(PDE5\) Inhibitors](#)

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Overview

This Coverage Policy addresses devices and procedures used in the treatment of erectile dysfunction.

Coverage Policy

Coverage for male sexual dysfunction varies across plans. Refer to the customer's benefit plan document for coverage details.

If coverage is available for the treatment of male sexual dysfunction, the following conditions of coverage apply.

Vacuum Constriction Device

A vacuum constriction device is considered medically necessary for the treatment of erectile dysfunction when there is failure, contraindication or intolerance to FDA approved pharmacological therapy (e.g., oral PDE5 inhibitors, intracavernosal injection, intraurethral medication).

A vacuum constriction device for ANY other indication is considered not medically necessary.

Penile Prosthesis

Surgical implantation of a penile prosthesis is considered medically necessary for the treatment of erectile dysfunction when ALL of the following criteria are met:

- erectile dysfunction has persisted for at least six months
- a comprehensive history and physical exam, including appropriate laboratory testing, has been completed
- there is failure, contraindication or intolerance to FDA pharmacological therapy (e.g., oral PDE5 inhibitors, intracavernosal injection, intraurethral medication)

Surgical reimplantation of a medically necessary penile prosthetic device, following the medically necessary removal of a penile prosthesis, is considered medically necessary when benefit coverage is available.

Removal of a penile prosthesis is considered medically necessary for ANY of the following indications:

- infection
- mechanical failure
- urinary obstruction
- intractable pain

A penile prosthesis for ANY other indication is considered not medically necessary.

Not Covered Procedures

Each of the following procedures for the treatment of erectile dysfunction is considered experimental, investigational or unproven:

- venous occlusive surgery (e.g., venous ligation)
- sural nerve grafting during radical retroperitoneal prostatectomy
- extracorporeal shock wave therapy (ESWT)

General Background

Erectile dysfunction (ED) (i.e., impotence) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance. ED usually has a physical cause in older men and is treatable at all ages. Although the incidence of ED increases with age, it is not an inevitable part of the aging process (Santucci and Bandukwala, 2016; Rosen, et al., 2005; Fazio, et al., 2004; Morales, 2003).

There are multiple causes of organic ED including disease processes, trauma, drug and alcohol use/abuse, as well as smoking. ED may occur as a result of an underlying medical condition, such as diabetes, kidney disease, hormonal imbalance, multiple sclerosis, atherosclerosis, vascular disease or neurological disease. Injury to the penis, spinal cord, prostate, bladder, and pelvis may also cause ED due to damage to nerves smooth muscles, arteries or fibrous tissue of the corpora cavernosa. Surgery, especially radical prostate or bladder surgery can injure the nerves and arteries near the penis resulting in ED. One of the side effects of medications, such as antihypertensive drugs, antihistamines, antidepressants, tranquilizers, histamine-receptor antagonists for treatment of gastric ulcers, opiates, and appetite suppressants is ED. Peyronie's disease, which causes scarring of the fibrous tissue of the penis, and priapism (i.e., persistent, abnormal erection of the penis) are also associated with ED. Other possible contributing factors of ED include smoking, which affects blood flow, and hormonal abnormalities. Psychological factors (e.g., stress, anxiety, depression, and low self-esteem) cause 10–

20% of ED cases (Santucci and Bandukwala, 2016; McVary, 2007; Rosen, et al., 2005; Fazio, et al., 2004; Morales, 2003).

Men with symptoms of ED should have a complete medical, sexual, and psychosocial history taken along with a physical examination and selective laboratory testing. Patients should be informed that ED is a risk factor for underlying cardiovascular disease and other health conditions that may warrant further evaluation and treatment. The laboratory tests that are routinely performed as a part of an ED evaluation are serum testosterone, glucose/hemoglobin A1c, and in some cases serum lipids. No routine serum study is likely to alter ED management. However, serum studies may provide information on the etiology of ED and reveal the presence of additional conditions that require treatment. In addition, a prostate specific antigen (PSA) may be appropriate in some men with ED (American Urological Association [AUA], 2018). Vascular flow to the corpora cavernosa may be evaluated using a penile doppler examination. Color duplex ultrasonography, which measures cavernous artery diameter and pressures, may also be used to assess venous leakage. According to the American Association of Clinical Endocrinologists (AACE), "occasionally, the measurement of nocturnal penile tumescence and rigidity is useful, especially to distinguish between psychologic and organic erectile dysfunction" (AACE, 2003).

The method of treatment for ED is dependent upon the etiology of the condition. Psychologically-based ED, without organic cause (e.g., secondary to depression, anxiety, stress) may dissipate with psychotherapy and/or behavioral therapy. Organic ED can occur as a secondary condition to several diseases and/or their treatment. Treatment of underlying diseases such as diabetes mellitus, hypertension, heart disease and endocrine conditions (e.g., hypogonadism, hyperprolactinemia, and thyroid disorders), and cessation or modification of prescription medications (e.g., antihypertensives) may be indicated. Discontinuing alcohol consumption and illicit drug use, and/or making lifestyle modifications (e.g., avoiding smoking, maintaining ideal body weight and engaging in regular exercise) may reverse ED. Treatment of Peyronie's disease resulting in severe curvature may involve the concomitant use of incision/grafting and prosthesis insertion due to the significant incidence of erectile dysfunction following surgery on the penis for Peyronie's plaques (Taylor and Levine, 2007). There is some controversy regarding testosterone replacement therapy, which includes oral preparations, intramuscular injections, topical gels, and transdermal preparations. Topical gels are the most commonly prescribed forms of testosterone replacement (Brant, et al., 2007; McVary, 2007; Seftel, et al., 2004; Morales, 2003).

Oral agents (e.g., PDE-5 inhibitors) have become the first-line treatment option for ED. Use of PDE-5 inhibitors is successful in 70–80% of men. With the availability of oral agents and minimally invasive options, surgical implantation typically occurs when these less invasive options are unavailable, unsuccessful or provide inadequate erectile function (Brant, et al., 2007; McVary, 2007; Sadeghi-Nejad, 2007; Jain and Terry, 2006; Carson, 2005; Fazio, et al., 2004; Morales, 2003). In addition to the surgically implanted prostheses, other procedures may be recommended for ED that is refractory to medical therapy. Vascular surgical procedures include penile arterial bypass or revascularization and venous ligation for the treatment of vasculogenic ED. For those with ED unresponsive to nonsurgical treatments, vascular surgery may be the preferred treatment option that offers the possibility of spontaneous, unaided erections. The success rates for arterial revascularization are low but reasonable success rates may be achieved in young, nonsmoking, otherwise healthy men with recently acquired ED due to a focal arterial occlusion. Techniques to improve the veno-occlusive mechanism with ligation of the dorsal, cavernous, and crural veins have been largely abandoned in favor of medical therapies (PDE-5 inhibitors) (Cunningham and Khera, 2016). Sural nerve grafting has been proposed as a surgical intervention for ED that occurs in association with radical prostatectomy. The Nesbit and Lue procedures are established for the correction of penile deformities caused by Peyronie's disease. Extracorporeal Shock Wave Therapy (ESWT) has also been proposed as a treatment for Peyronie's disease.

Non-pharmacologic Treatment of Erectile Dysfunction

Vacuum Constriction Device: When medical modalities are unsuccessful or contraindicated, a vacuum constriction device offers a viable alternative treatment. This device functions as an external aid; however, some users may find it difficult to use. The device causes an erection by creating a partial vacuum, drawing blood into the penis, engorging and expanding it. The device has three components: a plastic cylinder, in which the penis is placed; a pump that draws air out of the cylinder; and an elastic band that is placed around the base of the penis to maintain the erection when the cylinder is removed.

Penile Prosthesis: When nonsurgical therapies have proven ineffective, a penile prosthesis may be surgically implanted. Since surgery destroys the corpus cavernosum of the penis, this procedure precludes any future pharmacological treatment (Morales, 2003).

Complications of penile prostheses include erosion of the device, mechanical failure and the possibility of infection. Device extrusion, migration, urinary obstruction and prolonged or intractable pain are other potential risks. The average infection rate post-operatively ranges from 2–4% over a two year period, with most infections becoming evident during the first year. Some bacterial species can lie indolent for as long as two years before causing clinical signs of infection. Men with diabetes, spinal cord injuries or urinary tract infections have an increased risk of prosthesis-associated infections. If the infection cannot be successfully treated with antibiotics, it may be necessary to remove the prosthesis. Replacement with a new prosthesis should be delayed after removal of an infected prosthesis to allow adequate healing and eradication of the offending microorganism (Santucci and Bandukwala, 2016).

U.S. Food and Drug Administration (FDA)

There are two types of mechanical devices for treatment of erectile dysfunction: vacuum constriction devices and implantable penile prosthetic devices. Both are regulated by the FDA. Vacuum constriction devices are classified by the FDA as Class II medical devices and are exempt from the premarket notification requirements of the 510(k) process (FDA, 2004). Examples of these devices are the Rejoyn Vacuum Therapy System (Rejoyn Medical Systems, Nevada City, CA) and Osbon Erecaid™ Vacuum Therapy (Timm Medical Technologies, Dodge City, KS).

Implantable penile prostheses are either noninflatable (i.e., semirigid rods) or inflatable. Noninflatable devices are classified by the FDA as Class II medical devices and consist of a pair of semi-rigid rods or cylinders that are surgically implanted in the corpora cavernosa. The purpose of the device is to provide adequate penile rigidity for intercourse. This classification includes the following designs (FDA, 2000):

- rod prosthesis: a flexible, solid cylinder of polymer material
- malleable prosthesis: a flexible polymer cylinder that incorporates an internal metal core
- single-hinged prosthesis: a highly flexible material that enables the user to position the penis downward for concealment
- multiple-hinged prosthesis: a series of hinged segments, encapsulated in a polymer sheath

The Spectra™ (AMS Men's Health/Boston Scientific) and the Genesis® Penile Prosthesis (Coloplast, Minneapolis, MN) are examples of rigid penile prostheses.

Inflatable devices are classified by the FDA as Class III medical devices and consist of paired cylinders, surgically implanted inside the penis, which can be expanded using pressurized fluid. Tubes connect the cylinders to a reservoir filled with radiopaque fluid implanted in the abdomen and a subcutaneous pump implanted in the scrotum. The user inflates the cylinders by pressing on the small pump, located under the skin in the scrotum (FDA, 2017). The AMS 700™ (Boston Scientific) and the Titan® (Coloplast, Minneapolis, MN) are examples of inflatable penile prostheses.

Literature Review

Due to the nature of these devices, outcomes reported in studies evaluating their effectiveness are largely self-reported and subjective (e.g., patient satisfaction questionnaires). Objective outcome measures that have been reported in the medical literature include rate of mechanical failures and defects, and complications. Published evidence supports improved patient satisfaction with the use of penile implants when compared to sildenafil or intracavernous injections (Rajpurkar, et al., 2003); improved quality of life (Ferguson, et al., 2003); and improved erectile function (Mulhall, et al., 2003). Patient satisfaction has been reported to range from 71% to 91.2% with the use of implantable penile prostheses (Paranhos, et al., 2010; Knoll, et al., 2009; Israilov, et al., 2005; Minervini, et al., 2006; Zermann, et al., 2006; Ferguson, et al., 2003) Wilson et al. (2007) reported an estimated mechanical revision rate of 79.4% for device survival at 10 years compared to 71.2% at 15 years. The authors also noted with newer devices a 10-year mechanical survival and freedom from mechanical breakage increased to 88.6% and 97.9%, respectively. In general, the medical literature indicates these devices are safe and

effective for the treatment of ED for a carefully selected subset of individuals whose condition is organic in nature and have failed more conservative treatment.

Vascular Surgery

Patients who are considered for vascular surgical therapy typically have appropriate preoperative evaluation, which may include the combined injection and stimulation (CIS) test, dynamic infusion pharmaco-cavernosometry and cavernosography (DICC), duplex ultrasonography, and possibly arteriography. Penile arterial reconstructive surgery, also referred to as penile arterial bypass or revascularization, is one intervention that has the potential to cure patients with ED. During penile revascularization procedures, an arterial blockage is bypassed usually by anastomosing the inferior epigastric artery to the dorsal artery of the penis. Young men without other vascular risk factors (e.g., diabetes, high blood pressure, lipid disorders, cigarette smoking), who have ED due to pure artery blockage, are ideal candidates for this procedure. For posttraumatic arteriogenic ED in young patients, surgical penile revascularization has a 60–70% long-term success rate (Hatzimouratidis, et al., 2010).

Penile Vein Ligation

Venous ligation is a surgical procedure used to treat veno-occlusive ED, or erectile failure caused by venous insufficiency. The procedure involves the removal or ligation of the veins leaving the corpora cavernosa. Penile vein ligation techniques range from dorsal and accessory vein ligation to complete ligation and excision of the dorsal, cavernous, and crural veins. Surgery of the penile venous system has been reported to have some efficacy in patients with venous leakage. However, the tests necessary to establish this diagnosis have been incompletely validated. Therefore, it is difficult to select patients who will have a predictably good outcome. In general, the long-term benefits of venous ligation surgery have been limited. Success rates within the first year range from 23–80% but consistently decrease on longer follow-up (Rao and Donatucci, 2001).

Literature Review

Studies in the published peer-reviewed medical literature evaluating penile vein ligation for venogenic ED include case series primarily with small sample sizes. A larger series by Hsu et al. (2010) compared patients with veno-occlusive dysfunction who were treated with a venous stripping surgical method (n=178) with patients who were treated without this surgery (n=163). At an average follow-up of 7.7 years, there were no statistically significant differences in outcomes between the surgery and control groups as measured by the International Index of Erectile Function (IIEF-5) scores.

Cayan (2008) reported a series of 26 patients who underwent penile venous surgery with crural ligation for primary venous leakage. Postoperatively complete improvement in erectile function occurred in 11 men (42.3%), partial improvement occurred in eight (30.8%), and erectile function remained unchanged in seven (26.9%). Earlier case series have reported success rates of 31%–60% (Berardinucci, et al., 1996; Kim and McVary, 1995).

Sural Nerve Graft with Radical Prostatectomy

Despite advances in radical prostatectomy procedures, ED remains a significant postoperative complication. When both neurovascular bundles are spared during radical retropubic prostatectomy (RRP), potency rates of up to 70% have been reported, but rates of 30–60% have been observed. For intentional resection of both neurovascular bundles, the return of erectile function is the exception (Kim, et al., 2001). Sural nerve grafting has been proposed as an intervention at the time of RRP to prevent ED associated with the procedure. In sural nerve grafting, a portion of the sural nerve is harvested from one leg and then anastomosed to the divided ends of the cavernous nerves which are resected during a radical prostatectomy.

Literature Review

There is limited data in the scientific peer-reviewed literature regarding the long-term outcomes of sural nerve grafting. An RCT by Davis et al. (2009) compared outcomes of patients who underwent unilateral nerve-sparing radical prostatectomy with a sural nerve graft (n=66) to those who had unilateral nerve-sparing radical prostatectomy alone (n=41). At 24-month follow-up, there was no significant difference in the return of erectile function for the sural nerve graft group versus the control group (p=0.962).

Nonrandomized controlled comparison studies and case series have also evaluated the safety and effectiveness of sural nerve grafting with radical prostatectomy (Siddiqui, et al., 2014; Satkunasivam, et al., 2009; Hanson, et al., 2008; Zorn, et al., 2008; Sim, et al., 2006; Porpiglia, et al., 2005; Chang, et al., 2003; Kim, et al., 2001). Study populations have ranged from 28–40 with a follow-up range of 12–24 months. Small sample sizes have limited the generalizability of results. In addition, the results of these studies have not consistently shown a statistically significant difference in erectile function after sural nerve grafting.

Extracorporeal Shock Wave Therapy (ESWT)

ESWT is a noninvasive treatment that involves delivery of low- or high-energy shock waves via a device to a specific site within the body. These pressure waves travel through fluid and soft tissue; their effects occur at sites where there is a change in impedance, such as the bone/soft-tissue interface.

Peyronie's Disease (PD)

PD is a localized connective tissue disorder of unknown cause, and is characterized by the formation of inelastic fibrous plaques within the tunica albuginea or erectile tissue of the penis. For many patients, PD results in sexual problems due to the difficulty in attaining and/or maintaining erections. In a significant number of patients, the disorder improves or resolves spontaneously. Medical therapies, including antioxidants (such as vitamin E and potassium aminobenzoate) and corticosteroids injected directly into the plaque, lack adequate scientific support. Medical treatment options for PD typically include oral or intralesional drug therapy. Surgical management is considered for patients who have penile deformity compromising sexual function and whose PD has persisted for more than 12 months, and is refractory to medical therapy (Brant, et al., 2019).

ESWT has been investigated as a treatment option for PD. Various hypotheses about its mechanism of action exists, including direct damage to the plaque resulting in an inflammatory reaction with increased macrophage reaction leading to plaque lysis, improved vascularity resulting in plaque resorption, and the creation of contralateral scarring of the penis resulting in "false" straightening (Taylor and Levine, 2007). There is a lack of standardization regarding issues such as shockwave dosage, energy levels and number of sessions required for a therapeutic effect in patients with PD. Currently, the treatment of PD is not a U.S. Food and Drug Administration (FDA)-approved indication for ESWT.

Literature Review

The use of ESWT for the treatment of PD has been examined in several RCTs with a single systematic review/meta-analysis. Gao et al. (2016) conducted a meta-analysis of the evidence on ESWT for PD (n=6 studies/443 patients). Data was extracted from RCTS (n=3 studies/238 subjects), case-control studies (n=2 studies/111 subjects), and one cohort study (n=94 subjects). The primary outcomes were lessening of plaques and improvement of penile curvature. Secondary outcomes included relief and complete remission of pain, and improvement of sexual function. Follow-up ranged from four weeks to six months. Pooling data showed statistically significant pain relief and remission of pain ($p<0.0001$) after ESWT. A decrease of penile plaque was also observed ($p=0.02$). However, insignificant differences were found in improvement of penile curvature ($p=0.06$) and sexual function ($p=0.18$) between ESWT and placebo groups. A meta-analysis of RCTs only showed similar results for all parameters. Study limitations include the short-term follow-up in trials and the inclusion of low-quality evidence. The authors concluded that although the results of this meta-analysis suggests that ESWT may be an effective and relatively safe choice for PD patients with penile plaque and painful erection, the efficacy of ESWT could be very limited in patients with penile curvature and ED.

Chitale et al. (2010) randomized men with Peyronie's disease to receive ESWT (n=16) or sham (n=20). Inclusion requirements were stable penile deformity secondary to PD, recent onset of painless deformity of the penis on erection, and stable for > six months; pain and/or angulation of the penis on erection; difficult intercourse due to penile curvature, and partner dissatisfaction; a degree of ED (partial) associated with penile deformity; palpable plaque along the penis with penile deformity; aged > 18 years. The exclusion criteria were: congenital curvature of the penis; previous treatment for PD (surgical/medical); patients on warfarin and patients with total ED in need of therapy for ED. Primary outcome measures were the difference in the angle of deformity and the difference in IIEF score before and after treatment. Secondary outcome measures included the difference in VAS scores before and after treatment. At six months of follow-up there was no significant difference in the mean change between the control and intervention groups on any outcome measure. The study is limited by its small sample size. Results do not support the effectiveness of ESWT for PD.

Palmieri et al. (2009) conducted an RCT comparing ESWT as a treatment for PD with a duration of less than 12 months (n=50) to placebo (n=50). At 24 weeks, the mean visual analog scale (VAS) score was reported to be significantly lower in both groups compared to baseline. Mean plaque size and mean curvature degree were significantly higher in the placebo group compared to baseline and ESWT values. Study limitations include small sample size, restricted inclusion criteria, and short-term follow-up.

In general, the evidence evaluating the safety and efficacy of ESWT for PD consists of case series with relatively small sample sizes (n=44–157) and short-term follow-up (De Berardinis, et al., 2010; Poulakis, et al., 2006; Srirangam, et al., 2006; Strebel, et al., 2004; Hauck, et al., 2004). These studies have yielded inconsistent results.

Vasculogenic ED

Low-intensity ESWT (LI-ESWT) has recently been investigated as a treatment for patients with mild to severe ED resulting from altered blood flow to the penis. LI-ESWT is thought to induce mechanical stress and cellular microtrauma which results in the development of new blood vessels in the treated tissue of the corpora cavernosa. LI-ESWT aims to restore the erectile mechanism in order to enable natural or spontaneous erections. Patients who might be offered LI-ESWT include those with vasculogenic ED amenable to microvascular surgery.

Literature Review

Evidence in the published peer-reviewed medical literature evaluating ESWT for ED includes RCTs, cohort studies and systematic reviews/meta-analyses. Fojecki et al. (2017) assessed the outcome of linear low intensity-ESWT (LLi-ESWT) on ED at six and at 12 months from a randomized, double-blinded, sham-controlled trial. The advantage of linear ESWT compared with focused ESWT is that the usage of the linear probe delivers shock waves (SW) to a wider area of the corpora cavernosa, which limits movements of the probe during treatment. In this study, subjects with ED (n=126) were randomized into two groups to compare LLi-ESWT to sham treatment for ED. Group A (n=63) was assigned to a phase one sham for five weeks and phase two LLi-ESWT for five weeks. Group B (n=63) was assigned to phase one and phase two of LLi-ESWT (10 weeks). The inclusion criteria were; age over 40 years, complaints of ED and in a stable relationship for greater than six months. The primary outcome measure was an increase of at least five points in the IIEF-EF (Δ IIEF-EF score). The secondary outcome measure was an increase in the erectile hardness scale (EHS) score to at least a three in men with a score no higher than two at baseline. Patients (n=27) were excluded from final analysis for not returning questionnaires (n=23) or dropping out (n=4). Linear regression of the Δ IIEF-EF score from baseline to 12 months included 95 patients (n=95). The success rate based on the main outcome parameter (Δ IIEF-EF score \geq 5) was 54% in group A vs. 47% in group B (p=0.28). Improvements based on changes in the EHS score in groups A and B were 34% and 24%, respectively (p=0.82). The differences between groups were not clinically significant. The limitations of the study included the lack of dosage related studies and the study design. Only the short-term effects of sham treatment were assessed, because all participants received active treatment in the second phase. The authors concluded that exposure to two cycles of linear Li-ESWT for ED is not superior to one cycle at six and at 12-month follow-ups and further studies are needed.

Dong et al. (2019) conducted a systematic review and meta-analysis of seven randomized controlled trials (RCT's) (n=522 patients) to evaluate the efficacy of Li-ESWT by comparing the changes in the International Index of Erectile Function erectile function domain (IIEF-EF) and the Erection Hardness Score (EHS) to sham therapy in men with ED. The authors noted that men treated with Li-ESWT showed significant improvement in pooled mean IIEF-EF and EHS scores from baseline to follow-up compared to sham therapy (p<0.00001 and p<0.00001, respectively). Study limitations included small sample size, short term follow up and no unified protocol using Li-ESWT in treating ED. The authors concluded that additional well designed RCTs are needed in the future.

A systematic review and meta-analysis of 10 RCT's (n=873 patients) conducted by Sokolakis et al. (2019) concluded that when Li-ESWT was compared to sham, Li-ESWT significantly improved the IIEF-EF and EHS scores along with penile hemodynamics (p<0.0001, p=0.0009, p<0.00001, respectively). The mean follow-up was 5.12 months, with a range of 1–12 months. Acknowledged study limitations included the lack of consistency

in outcome measures, specified dose intensities (low, medium, high ESWT) and short-term follow-up. The study concluded that larger multi-centric RCTs with longer than one year follow-up are needed.

Kalyvianakis and Hatzichristou (2017) reported their results of a double-blinded, randomized, sham-controlled trial that assessed the effectiveness of low-intensity extracorporeal shockwave therapy (Li-ESWT) in patients with vasculogenic erectile dysfunction. Patients met inclusion criteria if they were at least 18 years old, had vasculogenic ED for at least six months, and were partial responders to PDE5 inhibitors. Following a four week washout period, the baseline International Index of Erectile Function erectile function domain (IIEF-EF) score had to be at least six (mild to moderate ED) to 21 (moderate and severe ED). Patients (n=46) were randomly assigned to receive Li-ESWT (n=30) or a sham procedure (n=16). All patients underwent penile triplex ultrasonography by the same investigator immediately before and three months after treatment. The primary outcome measured was the changes in peak systolic velocity and resistance index as measured by triplex ultrasonography at baseline and three months after treatment. Secondary outcomes measured were changes in the IIEF-EF score from baseline to one, three, six, nine, and 12 months after treatment and the percentage of patients reaching a minimal clinically important difference during the same period for the two groups. IIEF-EF minimal clinically important differences for the active vs sham group were observed for 56.7% vs 12.5% (p=0.005) at one month, 56.7% vs 12.5% (p=0.003) at three months, 63.3% vs 18.8% (p=0.006) at six months, 66.7% vs 31.3% (p=0.022) at nine months, and 75% vs 25% (p=0.008) at 12 months. Mean peak systolic velocity increased by 4.5 and 0.6 cm/s in the Li-ESWT and sham groups, respectively (p<0.001). Limitations included the small sample and strict inclusion criteria that do not reflect everyday clinical practice.

Clavijo et al. (2017) conducted a systematic review and meta-analysis of the evidence (n=7 RCTs/602 subjects) evaluating the efficacy of Li-ESWT for ED. RCTs were eligible for inclusion if they were published in the peer-reviewed literature and assessed erectile function outcomes using the IIEF-EF score. Estimates were pooled using random-effects meta-analysis. The average follow-up period was 19.8 weeks. A statistically significant improvement in pooled change in IIEF-EF score was found from baseline to follow-up in men undergoing Li-ESWT compared to those undergoing sham therapy (p<0.0001; between-group difference, p=0.047). Limitations of the review include the small sample size and short follow-up period in individual studies. It was also noted that data on PDE5i use during ESWT treatment was available in only five of seven studies. Although these results suggest that ESWT is more effective than sham therapy for ED, additional well-designed RCTs comparing ESWT to standard ED treatments are needed to establish the role in the treatment algorithm for ED.

Another systematic review and meta-analysis (n=14 studies/833 subjects) performed by Lu et al. (2017) evaluated the Li-ESWT for patients with ED. The evidence reviewed included RCTs (n=7 studies) which were used for meta-analysis and cohort studies (n=7 studies). No limitation was placed on the severity of ED or use of PDE-5i during treatment with Li-ESWT in studies. Follow-up occurred up to 12 months. The overall meta-analysis of the data showed that Li-ESWT improved the IIEF significantly overall in the treatment groups (p<0.0001). Different Li-ESWT setup parameters (energy flux density [EFD], number of pulses), and different treatment protocols, including treatment frequency and length of course, resulted in differences in reported efficacy. Results showed that studies using the highest EFD (> 0.2 mJ/mm²) reported significantly increased IIEFs (p<0.0001). Sub-group analysis (n=3 RCTs) showed that the IIEF of patients with mild ED increased significantly after Li-ESWT (p<0.0001), which did not occur for patients in the severe and moderate categories (p=0.30 and p=0.49, respectively). No adverse effects were reported. Acknowledged limitations of the meta-analysis were the inclusion of lower level evidence (i.e., cohort studies) and individual study deficiencies such as missing information as to details of randomization and treatment protocol.

Olsen et al. (2014) conducted a prospective, randomized blinded, placebo-controlled study (n=112) comparing LI-ESWT to sham treatment for ED. Both participants and physicians were blinded to treatment allocation. A total of 105 men with organic ED for at least six months who had responded to PDE-5 inhibitors were enrolled in this study. Additional inclusion requirements were an Erection Hardness Score (EHS) < 2 and an Index of Erectile Function (IIEF-15) score < 20. Exclusion criteria were psychogenic ED, neurological pathology and pelvic radiation or recovery from cancer within the past five years. The participants were assessed by EHS and IIEF-erectile function domain at baseline and at five weeks. Men in the placebo group (n=54) were offered LI-ESWT 10 weeks after study. The blinded part of the study was terminated at this point. The active placebo group (n=52) was assessed at five, 12 and 24 weeks after treatment. At five weeks of follow-up 29 men (57%) in the active group had an EHS of 3–4, which made it possible for them to have full sexual intercourse; three men (6%) had

an EHS of 1–2, and 19 (37%) showed no change in ED. In the placebo group, five men (9%) had an EHS of 3–4, seven (13%) an EHS of 1–2 and 42 (78%) had experienced no change. The difference between the two groups was statistically significant at the EHS levels 0 and 3–4 ($p=0.0001$). The EHS response rate was 80% at week 12 and 70% at week 24 in the active group. In the active placebo group, the EHS response rate was 85% at week 12 and 75% at week 24. Between weeks 12 and 24, the number of men who achieved improved EHS scores (3–4) decreased in both groups. There was no significant difference between the two groups in terms of IIEF-erectile function domain after week five. This study is limited by its short-term follow-up and unblinding after five weeks. Study results suggest a short-term treatment effect however, this effect was not maintained throughout the follow-up period.

Vardi et al. (2012) performed a randomized, double-blind, sham controlled study ($n=77$) of men with organic ED who were PDE-5 inhibitor responders. After a one-month PDE-5 inhibitor washout period, 67 men were randomized in a 2:1 ratio to receive 12 sessions of Li-ESWT ($n=40$) or sham therapy ($n=20$). The primary outcome was erectile function measured by the IIEF-EF, with treatment success defined as a 5-point or greater score improvement. Secondary outcomes included an increase in EHS and an improvement in penile blood flow. The 9-week treatment period was comprised of two treatment sessions per week for three weeks that were repeated after a three-week no treatment interval. Follow-up occurred one month after the final treatment session at which time erectile function and penile hemodynamics were reassessed while the men were still not taking PDE-5 inhibitors. At 13 weeks of follow-up, men in the treated group had a 5-point or greater increase in IIEF-EF than those in the sham group ($p=0.0001$). The treated men had significantly improved mean scores in the IIEF subcategories of Sexual Desire ($p=0.0348$) and Overall Satisfaction ($p=0.0054$). Penile hemodynamics improved significantly in the treated group ($p=0.0001$). Study limitations are short-term follow-up and small sample size. Additional data are needed to confirm the efficacy suggested by these results.

Although preliminary results appear promising, additional well-designed studies with long-term follow-up are needed to establish safety and effectiveness of ESWT for the treatment of ED.

Professional Societies/Organizations

American Academy of Family Physicians (AAFP): According to the AAFP, oral phosphodiesterase-5 inhibitors are the first-line treatments for ED. Second-line treatments include alprostadil, vacuum devices and when all other options are ineffective surgically implanted penile prostheses are an option (Rew et al., 2016).

American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE): AACE and ACE issued a guideline on the evaluation and treatment of male sexual dysfunction. The guideline supports the use of vacuum constriction pumps and internal implanted penile prostheses in the treatment of ED (AACE, 2003).

American Urological Association (AUA): In 2018, the AUA published revised guidelines on erectile dysfunction. According to the guidelines, men may choose to begin with the least invasive option, however any type of treatment as an initial treatment is a valid choice. The clinician is responsible to ensure that the man and his partner fully understand the benefits and risks/burdens associated with the choice and be informed of all the treatments (e.g., vacuum erection device, penile prosthesis) that are not contraindicated for the patient. The AUA also recommended against penile venous surgery and considered ESWT investigational.

National Comprehensive Cancer Network® (NCCN): According to the 2019 NCCN guidelines for prostate cancer, recovery of erectile function is directly related to factors such as age at radical prostatectomy, preoperative erectile function and the degree of preservation of the cavernous nerves. Replacement of resected nerves with nerve grafts has not been shown to be beneficial.

Centers for Medicare & Medicaid Services (CMS)

- National Coverage Determinations (NCDs): Diagnosis and Treatment of Impotence (230.4). This is a longstanding NCD; the effective date is not posted. The Coverage Policy is broader in scope than the NCD. Refer to the CMS NCD table of contents link in the reference section.
- Local Coverage Determinations (LCDs): Vacuum Erection Devices (VED) (L34824). The Coverage Policy is broader in scope than the LCD. Refer to the LCD table of contents link in the reference section.

Use Outside of the US

The Canada Urology Association (CUA) recommended a stepwise progression from oral agents through second- and third-line therapies. After reversible causes of ED are ruled out, the recommended first line therapy is a trial of oral medication. If oral treatment fails or if greater insight into the etiology is desired, then specialized testing and referral are done. The second-line therapies, although more invasive than oral agents, are generally well-tolerated and effective and include injection therapy, urethral therapy and vacuum erection device. Penile implant surgery remains the third-line therapy and is an important option for men refractory to medical management, offering effective and durable ED treatment outcomes (Bella, et al., 2015).

The European Association of Urology (EAU) guidelines on male sexual dysfunction states that if drug treatment fails, patients should be offered an alternative therapy such as intracavernosal injection therapy or the use of a vacuum erection device. The surgical implantation of a penile prosthesis may be considered in patients who do not respond to pharmacotherapy or who prefer a permanent solution to their problem. In regards to shockwave therapy and erectile dysfunction, the current data is still limited and clear recommendations cannot be given (Hatzimouratidis, et al., 2018).

In addition, the EAU guidelines on penile curvature state that the mechanism of action involved in extracorporeal shock wave lithotripsy is unclear. According to the EAU, extracorporeal shock wave treatment may only be used to treat penile pain (Hatzimouratidis, et al., 2018). However, the cited evidence supporting this statement consists of a single placebo-controlled RCT (Palmieri et al., 2009) described previously.

According to the National Institute for Health and Care Excellence (NICE), (2003), "current evidence on the safety of extracorporeal shockwave therapy (ESWT) for Peyronie's disease appears adequate. However, the evidence on the efficacy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research."

Coding/Billing Information

- Note:** 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Vacuum Constriction Device

Considered medically necessary when criteria in the applicable policy statements listed above are met and only when benefit coverage is available for the specific item:

HCPCS Codes	Description
L7900	Male vacuum erection system
L7902	Tension ring, for vacuum erection device, any type, replacement only, each

Penile Prosthesis

Considered medically necessary when criteria in the applicable policy statements listed above are met and only when benefit coverage is available for the specific service/item:

CPT® Codes	Description
54400	Insertion of penile prosthesis; non-inflatable (semi-rigid)
54401	Insertion of penile prosthesis; inflatable (self-contained)
54405	Insertion of multi-component, inflatable penile prosthesis, including placement of pump, cylinders, and reservoir

HCPCS Codes	Description
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C1813	Prosthesis, penile, inflatable
C2622	Prosthesis, penile, non-inflatable

Penile Prosthesis Removal

Considered medically necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
54406	Removal of all components of a multi-component, inflatable penile prosthesis without replacement of prosthesis
54408	Repair of component(s) of a multi-component, inflatable penile prosthesis
54410	Removal and replacement of all component(s) of a multi-component, inflatable penile prosthesis at the same operative session
54411	Removal and replacement of all components of a multi-component inflatable penile prosthesis through an infected field at the same operative session, including irrigation and debridement of infected tissue
54415	Removal of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis, without replacement of prosthesis
54416	Removal and replacement of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis at the same operative session
54417	Removal and replacement of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis through an infected field at the same operative session, including irrigation and debridement of infected tissue

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
37790	Penile venous occlusive procedure
55899†	Unlisted procedure, male genital system
64999††	Unlisted procedure, nervous system

†Note: Considered Experimental/Investigational/Unproven when used to report extracorporeal shock wave therapy for the treatment of erectile dysfunction.

††Note: Considered Experimental/Investigational/Unproven when used to report sural nerve grafting during radical retroperitoneal prostatectomy.

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