Varicose Veins

Number: 0050

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

I. Aetna considers the following procedures medically necessary for treatment of varicose veins when the following criteria are met: great saphenous vein or small saphenous vein ligation / division / stripping, radiofrequency endovenous occlusion (VNUS procedure), and endovenous laser ablation of the saphenous vein (ELAS) (also known as endovenous laser treatment (EVLT)).

A. Incompetence at the saphenofemoral junction or saphenopopliteal junction is documented by recent (performed within the past 6 months) Doppler or duplex ultrasound scanning, and all of the following criteria are met:

1. Ultrasound documented junctional reflux duration of 500 milliseconds (ms) or greater in the saphenofemoral or saphenopopliteal vein to be treated; and
2. Vein size is 4.5 mm or greater in diameter measured by ultrasound immediately below the saphenofemoral
or saphenopopliteal junction (not valve diameter at junction); and

3. Saphenous varicosities result in any of the following:

   a. Intractable ulceration secondary to venous stasis; or

   b. More than 1 episode of minor hemorrhage from a ruptured superficial varicosity; or a single significant hemorrhage from a ruptured superficial varicosity, especially if transfusion of blood is required; or

   c. Saphenous varicosities result in either of the following, and symptoms persist despite a 3-month trial of conservative management* (including analgesics and prescription gradient support compression stockings):

      i. Recurrent superficial thrombophlebitis; or

      ii. Severe and persistent pain and swelling interfering with activities of daily living and requiring chronic analgesic medication.

*Note: A trial of conservative management is not required for persons with persistent or recurrent varicosities who have undergone prior endovenous catheter ablation procedures or stripping/division/ligation in the same leg because conservative management is unlikely to be successful in this situation.

B. Surgical ligation (including subfascial endoscopic perforator vein surgery (SEPS)) or endovenous ablation procedures are considered medically necessary for the treatment of incompetent perforating veins with vein diameter measured by recent ultrasound of 3.5 mm or greater with outward flow duration of 500 milliseconds duration or more, located underneath an active or healed venous stasis ulcer (also known as CEAP C5 or C6) (see
Appendix).

C. Endovenous ablation procedures are considered medically necessary adjunctive treatment of symptomatic accessory saphenous veins for persons who meet medical necessity criteria for endovenous ablation above and who are being treated or have previously been treated by one of the procedures listed above for incompetence (i.e., reflux) at the saphenofemoral junction or saphenopopliteal junction and anatomically related persistent junctional reflux is demonstrated after the great or small saphenous veins have been removed or ablated.

*Note:* Initially, endovenous ablation therapy of the first vein and of the second and subsequent veins in each affected extremity is considered medically necessary when criteria are met. (Note: Thus one primary code and one secondary code for each affected leg are considered medically necessary for initial endovenous ablation treatment.) Additional endovenous ablation therapy is considered medically necessary for persons with persistent or recurrent junctional reflux of the greater saphenous vein, lesser saphenous vein following initial endovenous ablation therapy. (In order to authorize additional endovenous ablation, there should be documentation that the member continues to have symptoms and ultrasound showing persistent junctional reflux.) Additional endovenous ablation therapy may also be necessary for treatment of accessory saphenous veins as noted above. These procedures are considered experimental and investigational for treatment of varicose tributaries and accessory veins other than the accessory saphenous vein. These procedures are considered cosmetic for all other indications.

*Note:* Doppler or duplex ultrasound studies are considered necessary prior to varicose vein treatment to assess the anatomy and to determine whether there is significant reflux at the saphenofemoral or saphenopopliteal junction.
requiring surgical repair, and after completion of the
treatment to determine the success of the procedure and
detect thrombosis. Ultrasound guidance is inclusive of the
VNUS or ELAS procedures.

Note: The term endovenous catheter ablation (EVCA) is a
non-specific term that refers to the several catheter based
minimally invasive alternatives to surgical stripping such as
radiofrequency endovenous occlusion (VNUS procedure)
and endovenous laser ablation of the saphenous vein
(ELAS). In assessing the medical necessity of EVCA,
reference should be made to the specific technique that is
being employed.

II. Aetna considers liquid or foam sclerotherapy (endovenous
chemical ablation) (e.g., Varithena) medically necessary
adjunctive treatment of symptomatic saphenous veins,
varicose tributaries, accessory, and perforator veins 2.5 mm
or greater in diameter, measured by recent
ultrasound, for persons who meet medical necessity criteria
for varicose vein treatment in section I above and are being
treated or have previously been treated by one or more of
the procedures noted in section I above for incompetence
(i.e., reflux) at the saphenofemoral junction or
saphenopopliteal junction. Varithena has not been proven to
be more effective than other methods of foam
sclerotherapy.

Sclerotherapy is considered experimental and investigational
for treatment of reflux of the saphenofemoral junction or
saphenopopliteal junction because sclerotherapy has
not been proven to be effective for treatment of junctional
reflux. Sclerotherapy alone has not been shown to be
effective for persons with reflux at the saphenofemoral or
saphenopopliteal junctions; under established guidelines,
individuals with reflux should also be treated with
endovenous ablation, ligation or division of the junction to
reduce the risk of varicose vein recurrence. Sclerotherapy is
considered cosmetic for treatment of veins less than 2.5 mm
in diameter and for all other indications.

**Note:** Since ultrasound-monitored or duplex-guided techniques for sclerotherapy have not been shown to definitively increase the effectiveness or safety of this procedure, these tests are only considered medically necessary when initially performed to determine the extent and configuration of varicose veins. Ultrasound- or radiologically guided or monitoring techniques are of no proven value when performed solely to guide the needle or introduce the sclerosant into the varicose veins.

**Note:** The number of medically necessary sclerotherapy injection sessions varies with the number of anatomical areas that have to be injected, as well as the response to each injection. Usually 1 to 3 injections are necessary to obliterate any vessel, and 10 to 40 vessels, or a set of up to 20 injections in each leg, may be treated during one treatment session. Initially, up to two sets of injections of sclerosing solution in multiple veins in each affected leg (i.e., a total of four sets of injections if both legs are affected) are considered medically necessary when criteria are met. (Note: A set of injections is defined as multiple sclerotherapy injections during a treatment session.) Additional sets of injections of sclerosing solution are considered medically necessary for persons with persistent or recurrent symptoms.

III. Aetna considers ambulatory phlebectomy or transilluminated powered phlebectomy (TriVex System) medically necessary adjunctive treatment of symptomatic saphenous veins, varicose tributaries, accessory, and perforator veins 2.5 mm or greater in diameter for persons who meet the medical necessity criteria for varicose vein treatment in section I above and who are being treated or have previously been treated by one or more of the procedures noted in section I above for incompetence (i.e., reflux) at the saphenofemoral junction or saphenopopliteal junction. Ambulatory phlebectomy or transilluminated
powered phlebectomy is considered experimental and investigational for treatment of junctional reflux as these procedures have not been proven to be effective for these indications. Ambulatory phlebectomy and the TriVex system is considered cosmetic for veins less than 2.5 mm in diameter and all other indications. Note: Transilluminated powered phlebectomy has not been proven to be superior to other methods of varicose vein removal. Therefore, the TriVex procedure should be billed as any other varicose vein removal procedure.

Note: Initially, up to two multiple stab phlebectomy incisions in each affected extremity (i.e., a total of four multiple stab incisions if both legs are affected) are considered medically necessary when criteria are met. Additional multiple stab phlebectomy incisions are considered medically necessary for persons with persistent or recurrent symptoms. (Note: A set of stab phlebectomy incisions is defined as multiple stab phlebectomy incisions during a treatment session.)

IV. Aetna considers photothermal sclerosis (also referred to as an intense pulsed light source, e.g., the PhotoDerm VascuLight, VeinLase), which is used to treat small veins such as small varicose veins and spider veins, cosmetic because such small veins are cosmetic problems and do not cause pain, bleeding, ulceration, or other medical problems.

V. Aetna considers transdermal laser treatment experimental and investigational for the treatment of large varicose veins because it has not been proven in direct comparative studies to be as effective as sclerotherapy and/or ligation and vein stripping in the treatment of the larger varicose veins associated with significant symptoms (pain, ulceration, inflammation). Note: Although transdermal Nd:YAG laser has been shown to be effective for the treatment of telangiectasias and reticular veins, treatment of these small veins is considered cosmetic.

VI. Aetna considers endomechanical or mechanicochemical
ablation (MOCA) (e.g., ClariVein) experimental and investigational for varicose veins because it has not been proven to be as effective as established alternatives.

VII. Aetna considers Asclera polidocanol injection as cosmetic; although Asclera has been approved by the Food and Drug Administration (FDA) for the treatment of telangiectasias and reticular veins less than 3 mm in diameter, treatment of these small veins is considered cosmetic.

VIII. Aetna considers valvular reconstruction medically necessary for chronic venous insufficiency.

IX. Aetna considers micronized purified flavonoid fraction for the treatment of varicose veins experimental and investigational because its effectiveness has not been established.

X. Aetna considers the VeinGogh Ohmic Thermolysis System experimental and investigational because of insufficient evidence of its effectiveness.

XI. Aetna considers the medical adhesive (also referred to as cyanoacrylate superglue, n-butyl-cyanoacrylate) (e.g., VariClose Vein Sealing System, VenaSeal Closure System) for the treatment of varicose veins experimental and investigational because its effectiveness has not been established.

XII. Aetna considers polymorphism genotyping of matrix metalloproteinases genes (e.g., MMP1, MMP2, MMP3, and MMP7) as markers of predisposition to varicose veins experimental and investigational because the effectiveness of this approach has not been established.

XIII. Aetna considers synthetic matrix metalloproteinases inhibitors for the treatment of varicose veins experimental and investigational because its effectiveness has not been established.
For endoluminal cryoablation (also referred to as cryofreezing, cryostripping, cryosurgery, cryotherapy) for varicose veins, see CPB 0100 - Cryoablation (../100_199/0100.html).

**Background**

Varicose veins are a common condition. In adult western populations visible varicose veins are present in 20 to 25 % of women and 10 to 15 % of men. In most persons, varicose veins do not cause symptoms other than poor cosmesis. Varicose vein surgery is one of the most commonly performed cosmetic procedures in the United States.

Most varicose veins do not require medical treatment (Tapley et al, 2003). In some cases, however, the circulation may be hindered enough to cause swelling of the foot and ankle, discomfort, a tingling sensation, or a feeling of heaviness. For most people with varicose veins, wearing specially fitted elastic stockings is all that is needed. The stockings should be carefully fitted to the individual, providing the most pressure in the lowest part of the leg. The stockings should be put on when first arising in the morning, preferably before getting out of bed. Exercise such as walking or cycling also helps promote better circulation from the lower part of the body. Resting with the legs elevated will help promote circulation; in contrast, sitting with the legs crossed can aggravate the condition. Authorities have recommended 6 or more months as a reasonable duration for a trial conservative management (NHS, 2005).

A substantial proportion of varicose vein symptoms respond to conservative management. A randomized controlled clinical trial compared surgery (n = 124) to conservative management (n = 122) of varicose veins (Michaels et al, 2006). Conservative management consisted of lifestyle advice relating to exercise, leg elevation, management of weight and diet, and the use of compression hosiery. In the surgical arm of the trial patients received the same lifestyle advice but also underwent surgical treatment, consisting of flush ligation of sites of reflux, stripping
of the long saphenous vein and multiple phlebectomies, as appropriate. Although a greater proportion of patients assigned to surgery plus lifestyle advice at relieving symptoms at 1 year, approximately one-third of subjects assigned to conservative management reported some relief from conservative management with compression hosiery. At 2 years, there was no significant difference in symptom improvement between groups assigned to conservative management versus surgery. The authors posited that the lack of significant difference in symptomatology between groups at 2 years may have been due to cross-overs, with 7 patients in the conservative management group opting for surgery in year 1 and 37 patients opting for surgery in year 2. The study also found that persons assigned to surgery plus lifestyle advice had a greater improvement in cosmesis and quality of life than persons assigned to lifestyle advice alone, although it is not known whether improvements in quality of life were primarily related to improvements in cosmesis versus reductions in symptomatology. Weaknesses of the study included a substantial loss to follow-up in all groups. Fifteen of the 124 patients assigned to surgery either refused surgery in favor of conservative management or declined surgery due to fitness. Of the remaining 109 patients who underwent surgery, 43 were lost to follow up by the first year. Of subjects assigned to conservative treatment, 21 were lost to follow-up by the first year. The authors observed that, although surgery was more effective at improving symptomatology at 1 year, a substantial proportion of patients assigned to conservative treatment reported resolution or improvements in aching (26 %), heaviness (46 %), itching (56 %), and swelling (68 %). In addition, a substantial proportion of persons assigned to conservative management reported improvements in cosmesis. "Indeed, 22 % of the latter reported that they no longer had cosmetic concerns. These observations suggest a substantial benefit from surgery but perhaps support the case for careful evaluation of patients' symptoms and problems when considering surgical treatment."

An editorialist noted that the short follow-up of subjects
assigned to surgery may result in an underestimate of the costs and an exaggeration of the benefits of surgery (van Rij, 2006). By the third year, only 40% of subjects in the study by Michaels et al assigned to surgery were assessed. The editorialist noted, however, that most recurrences are diagnosed later than 3 years. Focusing on the short-term may lead to an underestimate of cost and an over-estimate of benefit. The editorialist stated that prospective comparisons of durability up to 5 years and longer are infrequent and yet by this time the recurrence rate may be as high as 50%.

In patients with varicose veins, leg pain may be associated with superficial thrombophlebitis or venous leg ulcers. In evaluating the role of varicose vein surgery in treatment of these conditions, the effectiveness of varicose vein surgery must be compared to conservative management.

If the patient is suffering from superficial thrombophlebitis, conservative management is indicated. According to available guidelines, uncomplicated superficial thrombophlebitis is usually treated symptomatically with heat, simple analgesia, non-steroidal anti-inflammatory drugs (NSAIDs), and compression stockings (SCHIN, 2002). Treatment should continue until symptoms have completely subsided (usually 2 to 6 weeks to subside but the thrombosed vein may be palpable and tender for months). More severe thrombophlebitis, as indicated by the degree of pain and redness and the extent of abnormality, should be treated by bed rest with elevation of the extremity and application of hot, wet compresses.

Leg ulcers arising from venous problems are called venous (varicose or stasis) ulcers. The main conservative treatment has been to apply a firm compression garment (bandage or stocking) to the lower leg in order to help the blood return back up the leg. Cullum et al (2002) conducted a meta-analysis of the literature on the effectiveness of compression bandaging and stockings in the treatment of varicose leg ulcers. The authors concluded that compression increases ulcer-healing rates compared with no compression. The authors also found
that multi-layered systems are more effective than single-layered systems. High compression is more effective than low compression but there are no clear differences in the effectiveness of different types of high compression. In a meta-analysis, Nelson et al (2002) found circumstantial evidence of the benefit of compression in reducing recurrence of varicose ulcers. The authors also noted that recurrence rates may be lower in high compression hosiery than in medium compression hosiery and therefore patients should be offered the strongest compression with which they can comply.

According to a systematic review of the evidence, pentoxifilline has also been shown to be effective for treatment of venous leg ulcers (Nelson et al, 2002). According to the systematic evidence review, compression has been shown to prevent venous leg ulcers. The effectiveness of vein surgery for prevention or treatment of venous ulcers is "unknown" (Nelson et al, 2002).

Beyond conservative therapy, the treatment of varicose veins in the lower legs includes injection/compression sclerotherapy and surgical stripping or ligation or a combination of these approaches depending upon the severity of the condition. Despite many years of experience, there is still a disappointingly high recurrence rate of varices because many patients are inadequately investigated before treatment. As it has been shown that physical examination alone is unreliable, pre-treatment Doppler or Duplex ultrasound examination must be performed for localization of the sites of incompetence to allow the individualization of the treatment strategy for each patient. Photographs or office diagrams may be helpful in assessing the size and extent of the varices.

Under established guidelines, the basic tenet of successful treatment is to eliminate the primary and secondary sources of the reflux. These sources are usually a nearby perforator, or most often a major junction that causes redirected venous return through veins with intact valves.
Sclerotherapy has been found to be more effective in patients with dilated superficial or residual varicose veins, recurrent varicosities or incompetent perforating veins of small to moderate size (less than 6 mm) without vein reflux. Large varicosities do not respond as well as small varicosities to sclerotherapy (Rosenberg, 2006; MSAC, 2011; MAS, 2011). Inadvertent intra-arterial injection has been an untoward sequela of sclerotherapy. Almost all cases of painful varicosities are associated with junctional reflux. When reflux at the saphenofemoral and/or saphenopopliteal junctions is present, accepted guidelines provide that sclerotherapy should not be performed until surgical ligation and division of the junction has been done. The junctions themselves can not be adequately treated by sclerotherapy as junctional reflux must be addressed by endovenous ablation methods or surgical ligation or stripping (Jakobsen, 1979; MSAC, 2008; MSAC, 2011). Although varicosities can occasionally be present in the absence or reflux, there is a lack of evidence from reliable clinical studies of the effectiveness of sclerotherapy in relieving symptomatic varicosities not associated with junctional reflux. The sole randomized controlled clinical trial (n = 25) to address the efficacy of sclerotherapy in varicosities not associated with junctional reflux (Kalhe and Leng, 2004) evaluated sclerotherapy efficacy in obliterating varicosities, but did not address its effectiveness at relieving pain. Although sclerotherapy can be used to treat visible subcuticular veins (i.e., spider angiomas, and telangiectasias) less than 2.5 mm in size, these small veins do not cause symptoms and their treatment is purely cosmetic (MSAC, 2011).

Doppler ultrasound is often used in conjunction with other non-invasive physiologic testing to characterize the anatomy and physiology of the varicose vein network prior to injection or surgical intervention. However, duplex scans are also sometimes utilized during the sclerotherapy procedure itself. Their purported usefulness in this regard includes the localization of deep or inaccessible injection sites, such as when there are extensive networks of large deep varicosities, areas of significant reflux between superficial and deep systems, or risks
Ultrasound has also been used to monitor the effectiveness of compressive sclerotherapy in obliterating the lumen of the target vein and reducing reflux/retrograde flow. However, these indications have not been scientifically validated. There is little evidence, in the form of randomized prospective clinical trials, to support that ultrasound makes a significant difference in optimizing outcome or decreasing complications, from sclerotherapy for varicose veins, when compared to non-ultrasound-guided techniques. A structured evidence review conducted by the Alberta Heritage Foundation for Medical Research (AHFMR) (2003) concluded that “the reviewed evidence does not adequately address the questions; which sclerosant is superior and which technique with or without ultrasound guidance is most efficacious.”

Venous reflux can be elicited manually by calf muscle compression and release, by the Valsava maneuver, or by pneumatic tourniquet release (Markovic & Shortell, 2014). If saphenofemoral reflux lasting longer than 500 ms is present, the diameter of the great saphenous veins (GSV) is recorded 2.5 cm distal to the saphenofemoral junction. The size of the vein has been correlated with the presence of significant saphenous reflux. The compliant GSV adjusts its luminal size to the level of transmural pressure, and measurement of its diameter has been shown to reflect the severity of hemodynamic compromise in limbs with GSV reflux. In a cohort study, Navarro, et al. (2002) evaluated the relationship of GSV diameter determined in the thigh and calf to clinical severity of reflux in 112 legs in 85 consecutive patients with saphenofemoral junction and truncal GSV incompetence. The authors stated that they found that the GSV diameter proved to be a relatively accurate measure of hemodynamic impairment and clinical severity in a model of saphenofemoral junction and GSV incompetence, predicting not only the absence of abnormal reflux, but also the presence of critical venous incompetence. A GSV diameter of 5.5 mm or less predicted the absence of abnormal reflux, with a sensitivity of 78 %, a specificity of 87 %, positive and negative predictive values of 78 %, and an accuracy of 82 %.
Ligation and division of the saphenofemoral and/or saphenopopliteal junction is indicated in patients with symptomatic varicose veins who have failed conservative management, when reflux of greater than 0.5 seconds is demonstrated by Doppler examination or Duplex scanning. The literature states that operative excision of varicose veins in the leg(s) should be reserved for those that are very large (greater than 6 mm), extensive in distribution, or occur in large clusters. Ligation alone usually results in a high recurrence rate of the varicose vein, which may then require sclerotherapy treatment (MSAC, 2008). Stripping of the greater and/or lesser saphenous vein, performed in conjunction with ligation and division of their respective junctions, is indicated when the saphenous veins themselves show varicose changes (usually greater than 1 cm in diameter). Varicose vein surgery and/or sclerotherapy during pregnancy is not appropriate because dilatation of veins in the legs is physiologic and will revert to normal after delivery, at which time a more accurate appraisal can be made. Visible subcuticular veins (i.e., spider angiomas, and telangiectasias) less than 2.5 mm in size do not cause symptoms and their treatment is purely cosmetic.

Ambulatory phlebectomy (AP) (also known as microphlebectomy) is a minimally invasive procedure performed under local anesthesia, and is an accepted outpatient therapy for the removal of varicose veins. This treatment allows excision of almost all of the large varicose veins except the proximal long saphenous vein, which is better-managed by stripping. Non-refluxing varicose veins on the surface of the leg, not including the saphenous veins, may be treated as an outpatient procedure under local anaesthetic using ambulatory phlebectomy (MSAC, 2011). However, recurrence rates can be high if the source of the reflux is not treated (MSAC, 2011). The junctions themselves can not be treated with simple phlebectomy as junctional reflux must be addressed by endovenous ablation methods or rarely by surgical ligation and stripping (MSAC, 2011; Weiss, 2007). Patients can ambulate immediately after AP. Complications associated with AP include blister formation, localized
thrombophlebitis, skin necrosis, hemorrhage, and persistent edema. The use of broad compression pads following AP reduces hemorrhage and enhances resorption.

The TriVex System (transilluminated powered phlebectomy) is an alternative method of providing ambulatory phlebectomy. This entails endoscopic resection and ablation of the superficial veins using an illuminator and a "powered vein rejector", a small powered surgical device. In this procedure, veins are marked with a magic marker. In order to enhance visualization of the veins, a bright light is introduced into the leg through a tiny incision. The powered vein rejector, which has a powered oscillating end, is then introduced to cut and dislodge the veins. The pieces of vein are then gently retrieved by suction down a tube. Transilluminated powered phlebectomy is usually performed in the hospital on an outpatient basis and under general anesthesia or using local anesthesia with sedation.

The manufacturer of the TriVex System states that the unique illumination feature allows the surgeon to quickly and accurately target and remove the vein and then visually confirm its complete extraction. The manufacturer claims that this new process makes varicose vein removal more effective, complete and less traumatic for patients, by reducing the number of incisions required to perform the procedure and the duration of surgery. The manufacturer also claims that this method not only reduces the pain associated with varicose vein removal but also reduces the potential for post-operative infection. There is inadequate evidence, however, in the published peer-reviewed medical literature substantiating these claims. The potential advantages of the TriVex System over standard ambulatory phlebectomy have not been proven. Therefore, the TriVex procedure should be billed as any other varicose vein removal procedure.

The term endovenous catheter ablation (EVCA) has been used to refer to the several new catheter based minimally invasive alternatives to surgical stripping, including laser ablation and radiofrequency ablation. Endovenous catheter ablation and
surgical ligation/stripping are indicated for treatment of the same general population: patients in whom the great and/or small saphenous veins have reflux or incompetence of 0.5 seconds or longer demonstrated on duplex scanning, and varicose vein symptoms significantly impinge on quality of life (MSAC, 2011). These patients have exhausted conservative treatment measures, and sclerotherapy is considered unlikely to provide successful results. Endovenous laser ablation and radiofrequency ablation are essentially identical except for the use of different specialized equipment and catheters, with thermal energy delivered through either a radiofrequency catheter or laser fiber (MSAC, 2011). The objectives of the two treatments are the same, being the destruction or ablation of a refluxing vein or segment of vein via application of thermal energy. The procedure to place the catheter within the vein is the same for radiofrequency ablation and endovenous laser ablation, also both procedures are conducted under duplex ultrasonography guidance (MSAC, 2011). The physiological mechanism of vein ablation is also the same, with thermal energy producing endothelial and vein wall damage, denaturing and occluding the vein to close the vein, abolishing venous reflux and visible varicosities (MSAC, 2011).

ECVA is performed with tumescent anesthesia (Markovic & Shortell, 2014). Tumescent anesthesia allows physicians to use large volumes (500 ml) of dilute (0.1%) lidocaine in a single session while achieving anesthesia levels equivalent to those achieved with 1% lidocaine. In this way, the entire thigh portion of the GSV can be safely anesthetized (and consequently obliterated) at one time. Epinephrine can be added to the solution to improve postoperative hemostasis, increase venous contraction around the heat-generating catheter, and lengthen the duration of postprocedural analgesia. A common formula for the tumescent anesthesia solution is 450 ml of normal saline mixed with 50 ml of 1% lidocaine with epinephrine (1:100,000 dilution) and 10 ml of sodium bicarbonate to buffer the acidity of the lidocaine.

Endovenous laser ablation of saphenous vein (ELAS) is a
treatment alternative to surgical ligation and stripping of the greater saphenous vein. Endovenous laser therapy for varicose veins is indicated for patients with clinically documented primary venous reflux, confirmed by duplex ultrasound, of the great or small saphenous veins (MSAC, 2008). Endovenous laser ablation is only suitable for patients with large, saphenous varicose veins, as the catheter requires saphenous veins with a minimum 4.5mm in diameter. These patients have exhausted other conservative treatment measures and sclerotherapy is considered unlikely to be successful (MSAC, 2008). After ultrasound examination to confirm the site and extent of saphenous reflux, a catheter is introduced into the damaged vein along a guide wire via percutaneous puncture at the distal extent of the diseased saphenous vein (MSAC, 2008). Perivascular infiltration of dilute local anesthetic along the length of the vein is then performed under ultrasound guidance to collapse the lumen and compress the vein onto the catheter, to dissipate heat generated during the procedure so as to prevent tissue damage, and to anesthetise the vein (MSAC). The guide wire is replaced with a laser probe introduced through the catheter to just below the saphenofemoral or saphenopopliteal junction, with positioning confirmed by ultrasound. Laser energy is then applied as the fiber and catheter are slowly withdrawn so as to close the vein and abolish venous reflux. Pulses of laser light are emitted inside the vein, and the vein collapses, and seals shut. This procedure may be performed in the office under local anesthesia. A bandage or compression hose is placed on the treated leg following the treatment. The procedure is performed on an outpatient basis.

Endovenous laser treatment can only be used for large veins, as a catheter must be inserted into the lumen of the vein to be treated (MSAC, 2008). Endovenous laser treatment is not viable on saphenous veins smaller than 4.5 mm in diameter, and cannot be used for the treatment of small veins or telangiectases. Smaller veins may be treated with sclerotherapy or ambulatory phlebectomy.
A range of laser wavelengths can be used to achieve occlusion; there is no strong evidence to indicate that any particular wavelength is superior to any other (MSAC, 2008). One systematic evidence review reported that the short term (within 6 months) reported occlusion rates of the GSV and small saphenous vein (SSV) found in studies of endovenous laser therapy were all greater than 90%.

Absolute contraindications to ELAS treatment include occlusive deep venous thrombosis and pregnancy. Relative contraindications include occlusive arterial disease, hypercoagulability, tortuous veins, and inability to ambulate (MSAC, 2008).

Endoluminal radiofrequency thermal heating (VNUS Closure Procedure) has been used with or without ligation and division for treatment of incompetence of the saphenofemoral and saphenopopliteal junction. To perform the radiofrequency ablation (RFA) procedure, the affected leg is prepared and draped, and a superficial local anaesthetic agent is used to anesthetize the site of cannulation. A radiofrequency catheter is inserted into the lumen of the greater saphenous vein, starting at its junction with the femoral vein. Under some protocols, the placement of the catheter is guided by duplex ultrasonography. The radiofrequency catheter heats the inner lumen of the vein to 85°C, with subsequent scarring and closure of the treated vein. The procedure is performed in an office setting without general anesthesia; treatment time averages 20 mins. Adverse sequelae include purpura, erythema and pain, which generally resolve days or weeks after treatment, and indurated fibrous cords that may remain for several months.

Upon completion of the RFA procedure, the site of venous puncture is dressed, and compression stockings and/or bandages are applied as appropriate to reduce the risk of venous thromboembolism and to reduce postoperative bruising and tenderness (MSAC, 2011). Non-steroidal anti-inflammatory drugs are commonly used for post-procedural pain relief. For most patients additional procedures such as sclerotherapy or
Phlebectomy are required for the treatment of superficial veins below the knee, any tributary varicose veins, and telangiectases. These procedures may be performed during the RFA or endovenous laser treatment procedure, or over one or two follow-up visits.

Radiofrequency ablation is designed as a single-use therapeutic intervention, delivered as a single course of treatment per affected leg to obliterate the great or small saphenous veins through the application of thermal energy (MSAC, 2011). While generally indicated for primary varicose veins, re-treatment of varicose veins with RFA may be possible in some patients where neovascularisation or revascularisation has occurred. However, revascularization in the short term following treatment is uncommon. Studies reporting on radiofrequency ablation with the more efficient second generation catheters report ablation rates close to 100% at 6-month follow-up with no major adverse events (MAS, 2011).

Prospective case series extending to 24 months have shown success rates with RFA similar to those reported for vein ligation and stripping. Weiss and Weiss (2002) reported complete disappearance of the treated saphenous vein in 90% of 21 patients followed for 24 months. Endothermal radiofrequency thermal heating may be performed with or without high ligation of the greater saphenous vein. Chandler et al (2000) found no statistically significant difference in 1-year success rates from endovenous radiofrequency catheter ablation in 120 limbs treated without saphenofemoral ligation and 60 limbs treated with saphenofemoral ligation. The authors concluded that "these early results suggest that extended saphenofemoral junction (SFJ) ligation may add little to effective GSV [greater saphenous vein] obliteration, but our findings are not sufficiently robust to warrant abandonment of SFJ ligation as currently practiced in the management of primary varicose veins associated with GSV reflux."

Pivotal studies of endovenous catheter ablation (endovenous laser ablation and endovenous radiofrequency...
Ablation (ablation) procedures have focused on junctional incompetence. There is a lack of evidence of the effectiveness of endovenous catheter ablation procedures for treatment of varicose tributaries and perforator veins. In addition, there are no studies comparing endovenous catheter ablation procedures to standard methods of treating varicose tributaries and perforator veins with sclerotherapy and ambulatory phlebectomy.

The Society for Interventional Radiologists (2003) has a position statement on VNUS that states that “(d)uplex ultrasound is necessary to map the anatomy of the venous system prior to the procedure, and imperative during the procedure for correct catheter placement and for proper tumescent anesthetic administration to minimize potential complications. Duplex ultrasound also is necessary for follow-up after endovenous ablation.”

Sadick (2000) has noted that the new less-invasive technologies for treatment of varicose veins must be evaluated with caution. "Long-term studies with other technologies must be compared with surgical ligation of the incompetent SFJ (saphenofemoral junction). Six-month and 5-year follow-ups are two different end points. The latter is a more accurate time interval of therapeutic efficacy."

Subfascial endoscopic perforator vein surgery (SEPS) is a minimally invasive endoscopic procedure that eliminates the need for a large incision in the leg. It has been explored as an alternative to the traditional open surgical treatment of chronic venous insufficiency. The aim of the procedure is to interrupt incompetent medial calf perforating veins to reduce venous reflux and decrease ambulatory venous hypertension in critical areas above the ankle where venous ulcers most frequently develop. Kalra and Gloviczki (2002) stated that available evidence confirmed the superiority of SEPS over open perforator ligation, but do not address its role in the surgical treatment of advanced chronic venous insufficiency (CVI) and venous ulceration. Ablation of superficial reflux by high ligation
and stripping of the greater saphenous vein with avulsion of branch varicosities is concomitantly performed in the majority of patients undergoing SEPS. The clinical and hemodynamic improvements attributable to SEPS thus are difficult to ascertain. As with open perforator ligation, clinical and hemodynamic results are better in patients with primary valvular incompetence (PVI) than in those with the post-thrombotic (PT) syndrome. Until prospective, randomized, multicenter clinical studies are performed to address lingering questions regarding the effectiveness of SEPS, the procedure is recommended in patients with advanced CVI secondary to PVI of superficial and perforating veins, with or without deep venous incompetence. The performance of SEPS in patients with PT syndrome remains controversial.

Contraindications for SEPS include associated arterial occlusive disease, infected ulcer, a non-ambulatory patient, and a medically high-risk patient. Diabetes, renal failure, liver failure, morbid obesity, ulcers in patients with rheumatoid arthritis, or scleroderma, and presence of deep vein obstruction at the level of the popliteal vein or higher on pre-operative imaging are relative contraindications. Patients with extensive skin changes, circumferential large ulcers, recent deep vein thrombosis, severe lymphedema, or large legs may not be suitable candidates (Kalra and Gloviczki, 2002).

McDonagh et al (2002, 2003) has reported on the effectiveness of ultrasound-guided foam sclerotherapy (comprehensive objective mapping, precise image-guided injection, anti-reflux positioning and sequential sclerotherapy (COMPASS) technique) in the treatment persons with varicosities of the greater saphenous vein with saphenous vein reflux. Published studies of the COMPASS technique involve relatively short-term follow up. Study subjects were followed for 3 years, and for only 2 years after completion of a series of repeat sclerotherapy injections that were administered over 1 year. In addition, these studies do not include a comparable group of subjects treated with surgery, which has been the primary method of treating incompetent long saphenous veins. Thus, it is not
possible to reach definitive conclusions about the durability of results of the COMPASS technique or its effectiveness compared with surgery for treatment of greater saphenous vein varicosities and saphenofemoral incompetence. In addition, published studies of the COMPASS technique come from a single group of investigators. In reviewing the study by McDonagh (2002), Allegra (2003) commented: “Surgical treatment has a long history with 5-20 year follow-ups being routine. The 3 year follow-up in the present study is certainly not comparable .... This study does not answer questions raised against ultrasound guided sclerotherapy. It would be important to have the relevant aspects of this study duplicated, reproduced, and verified.”

Published long-term randomized controlled clinical studies have demonstrated that surgery plus sclerotherapy is more effective than surgery alone for treatment of varicosities associated with incompetence of the saphenofemoral junction. Belcaro et al (2003) reported on the results from the Venous Disease International Control (VEDICO) trial, the first long-term randomized controlled clinical trial of foam sclerotherapy. The VEDICO trial involved 749 patients with varicose veins and saphenous vein incompetence who were randomly treated by six different approaches: standard sclerotherapy, high-dose sclerotherapy, surgical ligation, stab avulsion, foam sclerotherapy, and combined surgery (ligation or stab avulsion) and high dose sclerotherapy. At 10 years, the occurrence of new veins was 56% for standard sclerotherapy, 51% for foam sclerotherapy, 49% for high-dose sclerotherapy, 41% for stab avulsion, 38% for ligation, and 27% for combined surgery and sclerotherapy.

Belcaro et al (2000) reported on the results of a randomized controlled clinical study comparing ultrasound-guided sclerotherapy with surgery alone or surgery combined with sclerotherapy in 96 patients with varicose veins and superficial venous incompetence. Although all approaches were reported to be effective in controlling the progression of venous incompetence, surgery appeared to be the most effective
method on a long-term basis, and that surgery combined with sclerotherapy may be more effective than surgery alone. After 10 years follow-up, no incompetence of the saphenofemoral junction was observed in both groups assigned to surgery, compared to 18.8% of limbs of subjects assigned to ultrasound-guided sclerotherapy. Of limbs treated with ultrasound-guided sclerotherapy, 43.8% of the distal venous systems were incompetent, compared to 36% of limbs of subjects treated with surgery alone, and 16.1% of limbs of subjects treated with surgery plus sclerotherapy.

The L'Agence Nationale d'Accréditation et d'Evaluation en Sante (l'ANAES) (Grange et al, 1998) conducted a systematic review of the literature on the indications of surgery for varicose veins of the legs. Given the lack of good scientific evidence on the various treatments for primary varicose veins, the working group made recommendations based on professional agreement. They concluded that surgery is the treatment of choice for saphenous veins with reflux. An evidence review of surgical treatments for deep venous incompetence by the Alberta Heritage Foundation for Medical Research (Scott and Corabain, 2003) stated that "(s)cierotherapy is particularly effective in superficial venous incompetence when there is a large vein located in close proximity to the ulcer. However, surgery is indicated when there is substantial proximal incompetence in a saphenous vein."

A comprehensive evidence review of sclerotherapy for varicose veins conducted by the Alberta Heritage Foundation for Medical Research (2003) concluded that "the reviewed evidence does not adequately address the questions; which sclerosant is superior and which technique with or without ultrasound guidance is most efficacious ... In recent years, new methods such as ES (endovascular sclerotherapy) and foam sclerotherapy (using ultrasound guidance) have been developed and proposed to improve the safety and efficacy of sclerotherapy for various types of varicose veins. Evidence about these new techniques for treating patients with incompetence of the long saphenous vein is limited." The
assessment concluded that although "(s)clerotherapy appears to be the treatment of choice for reticular varicosities, telangiectasia and other small, unsightly blood vessels ... (t)he place of sclerotherapy as the first treatment for larger varicose veins (saphenous or non-saphenous) remains controversial."

There is a lack of reliable evidence that one type of sclerosant is significantly better than any other (Tisi 2007; Jia et al, 2006). Jia and colleagues (2007) evaluated the safety and effectiveness of foam sclerotherapy for varicose veins. The authors concluded that serious adverse events associated with foam sclerotherapy are rare. However, there is insufficient evidence to allow a meaningful comparison of the effectiveness of this treatment with that of other minimally invasive therapies or surgery.

Kendler and associates (2007) noted that "(r)ecently the use of foam sclerotherapy had a renaissance. Several studies have documented the efficacy of foam sclerotherapy in selected patients. The possibility of treating patients in an outpatient setting, with low costs and rapidly, makes foam sclerotherapy very attractive compared to invasive and minimally invasive methods. However long-term follow-ups in properly controlled randomized trials are needed before foam sclerotherapy can be recommended as a routine procedure".

The FDA has approved Asclera (polidocanol) injection (BioForm Medical Inc., Franksville, WI) to close spider veins (tiny varicose veins less than 1 millimeter in diameter) and reticular veins (those that are 1 to 3 millimeters in diameter). As these small veins have not been demonstrated to cause symptoms, treatment of these small veins is considered cosmetic.

There is emerging evidence for the Ambulatory Conservative Hemodynamic Management of Varicose Veins (CHIVA) method. In an open-label, randomized controlled trial, Pares and colleagues (2010) compared the effectiveness of the Ambulatory Conservative Hemodynamic Management of Varicose Veins (CHIVA) method for the treatment of varicose veins with respect to the standard treatment of stripping.
According to the authors, CHIVA consists of minimally invasive surgical procedures under local anesthesia that are based on hemodynamic analysis of the legs with pulsed Doppler ultrasound. A total of 501 adult patients with primary varicose veins were treated in a single center. They were assigned to an experimental group, the CHIVA method (n = 167) and 2 control groups: stripping with clinic marking (n = 167) and stripping with Duplex marking (n = 167). The outcome measure was clinical recurrence within 5 years, assessed clinically by previously trained independent observers. Duplex ultrasonography was also used to assess recurrences and causes. In an intention-to-treat analysis, clinical outcomes in the CHIVA group were better (44.3 % cure, 24.6 % improvement, 31.1 % failure) than in both the stripping with clinic marking (21.0 % cure, 26.3 % improvement, 52.7 % failure) and stripping with Duplex marking (29.3 % cure, 22.8 % improvement, 47.9 % failure) groups. The ordinal odds ratio between the stripping with clinic marking and CHIVA groups, of recurrence at 5-year follow-up, was 2.64, (95 % confidence interval (CI): 1.76 to 3.97, p < 0.001). The ordinal odds ratio of recurrence at 5-year follow-up, between the stripping with Duplex marking and CHIVA group, was 2.01 (95 % CI: 1.34 to 3.00, p < 0.001). The authors concluded that these findings indicated that the CHIVA method is more effective than stripping with clinical marking or stripping with Duplex marking to treat varicose veins. Furthermore, when carrying out a stripping intervention, Duplex marking does not improve the clinical results of this ablative technique.

In a randomized study, Rasmussen et al (2011) compared 4 treatments for varicose GSVs. A total of 500 consecutive patients (580 legs) with GSV reflux were randomized to endovenous laser ablation (EVLT, 980 and 1,470 nm, bare fiber), radiofrequency ablation (RFA), ultrasound-guided foam sclerotherapy (USGFS) or surgical stripping using tumescent local anesthesia with light sedation. Mini-phlebectomies were also performed. Patients were examined with duplex imaging before surgery, and after 3 days, 1 month and 1 year. At 1 year, 7 (5.8 %), 6 (4.8 %), 20 (16.3 %) and 4 (4.8 %) of the GSVs
were patent and refluxing in the laser, radiofrequency, foam and stripping groups respectively \( (p < 0.001) \). One patient developed a pulmonary embolus after foam sclerotherapy and 1 a deep vein thrombosis after surgical stripping. No other major complications were recorded. The mean (S.D.) post-intervention pain scores (scale 0 to 10) were 2.58 (2.41), 1.21 (1.72), 1.60 (2.04) and 2.25 (2.23), respectively \( (p < 0.001) \). The median (range) time to return to normal function was 2 (0 to 25), 1 (0 to 30), 1 (0 to 30) and 4 (0 to 30) days, respectively \( (p < 0.001) \). The time off work, corrected for weekends, was 3.6 (0 to 46), 2.9 (0 to 14), 2.9 (0 to 33) and 4.3 (0 to 42) days, respectively \( (p < 0.001) \). Disease-specific quality-of-life and Short Form 36 (SF-36) scores had improved in all groups by 1-year follow-up. In the SF-36 domains bodily pain and physical functioning, the radiofrequency and foam groups performed better in the short-term than the others. The authors concluded that all treatments were efficacious. The technical failure rate was highest after foam sclerotherapy, but both RFA and foam were associated with a faster recovery and less post-operative pain than EVLT and stripping.

In a Cochrane review, Nesbitt et al (2011) reviewed available randomized controlled trial (RCT) data comparing USGFS, RFA and EVLT to conventional surgery (high ligation and stripping (HL/S)) for the treatment of great saphenous varicose veins. The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialised Register (July 2010) and CENTRAL (The Cochrane Library 2010, Issue 3). In addition the authors performed a search of EMBASE (July 2010). Manufacturers of EVLT, RFA and sclerosant equipment were contacted for trial data. All RCTs of EVLT, RFA, USGFS and HL/S were considered for inclusion. Primary outcomes were recurrent varicosities, re-canalization, neovascularization, technical procedure failure or need for re-intervention, patient quality of life (QoL) scores and associated complications. Secondary outcomes were type of anesthetic, procedure duration, hospital stay and cost. A total of 13 reports from 5 studies with a combined total of 450 patients were included. Rates of re-canalization were higher following EVLT compared with HL/S, both early (within four
months) (5/149 versus 0/100; odds ratio (OR) 3.83, 95% CI: 0.45 to 32.64) and late re-canalization (after 4 months) (9/118 versus 1/80; OR 2.97 95% CI: 0.52 to 16.98), although these results were not statistically significant. Technical failure rates favored EVLT over HL/S (1/149 versus 6/100; OR 0.12, 95% CI: 0.02 to 0.75). Recurrence following RFA showed no difference when compared with surgery. Re-canalization within 4 months was observed more frequently following RFA compared with HL/S although not statistically significant (4/105 versus 0/88; OR 7.86, 95% CI: 0.41 to 151.28); after 4 months no difference was observed. Neovascularization was observed more frequently following HL/S compared with RFA, but again this was not statistically significant (3/42 versus 8/51; OR 0.39, 95% CI: 0.09 to 1.63). Technical failure was observed less frequently following RFA compared with HL/S although this was not statistically significant (2/106 versus 7/96; OR 0.48, 95% CI: 0.01 to 34.25). No RCTs comparing HL/S versus USGFS met the study inclusion criteria. QoL scores and operative complications were not amenable to meta-analysis. The authors concluded that currently available clinical trial evidence suggests RFA and EVLT are at least as effective as surgery in the treatment of great saphenous varicose veins. There are insufficient data to comment on USGFS. They stated that further randomized trials are needed; and they should aim to report and analyze results in a congruent manner to facilitate future meta-analysis.

Mueller and Raines (2013) stated that the ClariVein system is the first venous ablation technique to employ a hybrid (dual-injury) technique built into 1 catheter-based delivery system. Endo-mechanical abrasion is produced by the tip of the catheter's rotating wire (mechanical component); and EVCA is via simultaneous injection of sclerosant over the rotating wire (chemical component). The author was an early adopter of this technique and via experience has developed a detailed step-by-step protocol. To date, there have been 2 pivotal clinical studies published using the ClariVein system. These data were compared with the results using other methods of endovenous ablation. The authors concluded that the ClariVein system has the potential to become a first-line treatment.
Lawson et al (2013) noted that less invasive endovenous techniques have been shown to be as effective as open surgery in the treatment of varicose veins. Furthermore, they cause less post-operative bruising and pain and enable early return to normal activities and work. Tumescent anesthesia is safe and obviates complications of general or spinal anesthesia. Drawbacks are a steep learning curve and painful administration during treatment. Tumescentless techniques like ClariVein or VenaSeal Sapheon Closure System are recently under investigation. Short-term results of VenaSeal are comparable with thermal ablation. The procedure is safe without serious adverse events. Peri-operative pain and patient discomfort with this tumescentless approach is minimal but post-operative recovery is temporarily hindered by thrombophlebitis in 14 to 15% of patients. One-year results in a small feasibility study has demonstrated durable closure at this end-point. No longer-term results are available. A randomized control trial between VenaSeal and Covidien ClosureFast is in a preparatory phase.

A randomized controlled trial comparing foam sclerotherapy to laser ablation and surgery found that laser ablation and surgery had better outcomes, and that laser had the fewest procedural complications. Brittenden et al (2014) stated that ultrasound-guided foam sclerotherapy and endovenous laser ablation are widely used alternatives to surgery for the treatment of varicose veins, but their comparative effectiveness and safety remain uncertain. In a randomized trial involving 798 participants with primary varicose veins at 11 centers in the United Kingdom, these researchers compared the outcomes of foam, laser (laser ablation of truncal saphenous veins, followed if needed by foam sclerotherapy) and surgical treatments (proximal ligation and stripping of the great saphenous vein with concurrent phlebectomy). Study participants had varicose veins larger than 3 mm in diameter and reflux of the saphenous veins of more than 1 second by duplex ultrasound. The participants mean age was 49 years, 57% were women, and approximately 30% had bilateral varicose veins. Those with recurrent varicose veins after previous treatment
were excluded. Primary outcomes at 6 months were disease-specific quality of life and generic quality of life, as measured on several scales. Secondary outcomes included complications and measures of clinical success. After adjustment for baseline scores and other covariates, the mean disease-specific quality of life was worse after treatment with foam than after surgery (p = 0.006) but was similar in the laser and surgery groups. There were no significant differences between the surgery group and the foam or the laser group in measures of generic quality of life. At 6 months, approximately 80% of patients in the laser and surgery groups showed complete ablation of the great saphenous vein on duplex ultrasound, compared with only 43% in the foam group (p < 0.001). The frequency of procedural complications was similar in the foam group (6%) and the surgery group (7%); but was lower in the laser group (1%) than in the surgery group (p < 0.001); the frequency of serious adverse events (approximately 3%) was similar among the groups. At 6 months, lumpiness and staining of the skin were somewhat more common in the foam group.

On November 26, 2013, the FDA approved Varithena (polidocanol injectable foam) for the treatment of patients with incompetent veins and visible varicosities of the great saphenous vein (GSV) system. The prescribing information states: "Varithena (polidocanol injectable foam) is indicated for the treatment of incompetent great saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous vein (GSV) system above and below the knee. Varithena improves the symptoms of superficial venous incompetence and the appearance of visible varicosities." Although the FDA approval does not exclude use of Varithena foam sclerotherapy for treatment of SF or SP; junctional reflux, there are a lack of studies comparing Varithena to endovenous ablation procedures for SF or SP junctional reflux. In addition, there is a paucity of evidence examining the long-term durability of results of Varithena treatment of junctional reflux.

Todd et al (2014) reported on a RCT to determine efficacy and safety of polidocanol endovenous microfoam in treatment of
symptoms and appearance in patients with saphenofemoral junction incompetence due to reflux of the great saphenous vein or major accessory veins. Patients were randomized equally to receive polidocanol endovenous microfoam 0.5 %, polidocanol endovenous microfoam 1.0 % or placebo. The primary efficacy end-point was patient-reported improvement in symptoms, as measured by the change from baseline to Week 8 in the 7-day average electronic daily diary VVSymQ™ score. The co-secondary end-points were the improvement in appearance of visible varicosities from baseline to Week 8, as measured by patients and by an independent physician review panel. In 232 treated patients, polidocanol endovenous microfoam 0.5 % and polidocanol endovenous microfoam 1.0 % were superior to placebo, with a larger improvement in symptoms (VVSymQ (-6.01 and -5.06, respectively, versus -2.00; p < 0.0001) and greater improvements in physician and patient assessments of appearance (p < 0.0001). These findings were supported by the results of duplex ultrasound and other clinical measures. Of the 230 polidocanol endovenous microfoam-treated patients (including open-label patients), 60 % had an adverse event compared with 39 % of placebo; 95 % were mild or moderate. No pulmonary emboli were detected and no clinically important neurologic or visual adverse events were reported. The most common adverse events in patients treated with polidocanol endovenous microfoam were retained coagulum, leg pain and superficial thrombophlebitis; most were related to treatment and resolved without sequelae.

Brittenden and colleagues (2015) stated that foam sclerotherapy (foam) and endo-venous laser ablation (EVLA) have emerged as alternative treatments to surgery for patients with varicose veins (VV), but uncertainty exists regarding their effectiveness in the medium to longer term. These investigators evaluated the clinical effectiveness and cost-effectiveness of foam, EVLA and surgery for the treatment of VV. A total of 798 patients with primary VV (foam, n = 292; surgery, n = 294; EVLA, n = 212) were included in this study. Patients were randomized between all 3 treatment options (8 centers) or between foam and surgery (3 centers). Primary
outcome measures included disease-specific [Aberdeen Varicose Vein Questionnaire (AVVQ)] and generic [European Quality of Life-5 Dimensions (EQ-5D), Short Form questionnaire-36 items (SF-36) physical and mental component scores] quality of life (QoL) at 6 months. Cost-effectiveness as cost per quality-adjusted life-year (QALY) gained. Secondary outcome measures entailed QoL at 6 weeks; residual VV; Venous Clinical Severity Score (VCSS); complication rates; return to normal activity; truncal vein ablation rates; and costs. The results appeared generalizable in that participants' baseline characteristics (apart from a lower-than-expected proportion of females) and post-treatment improvement in outcomes were comparable with those in other RCTs. The health gain achieved in the AVVQ with foam was significantly lower than with surgery at 6 months [effect size -1.74, 95% CI: -2.97 to -0.50; p = 0.006], but was similar to that achieved with EVLA. The health gain in SF-36 mental component score for foam was worse than that for EVLA (effect size 1.54, 95% CI: 0.01 to 3.06; p = 0.048) but similar to that for surgery. There were no differences in EQ-5D or SF-36 component scores in the surgery versus foam or surgery versus EVLA comparisons at 6 months. The trial-based cost-effectiveness analysis showed that, at 6 months, foam had the highest probability of being considered cost-effective at a ceiling willingness-to-pay ratio of £20,000 per QALY. EVLA was found to cost £26,107 per QALY gained versus foam, and was less costly and generated slightly more QALYs than surgery. Markov modelling using trial costs and the limited recurrence data available suggested that, at 5 years, EVLA had the highest probability (approximately 79%) of being cost-effective at conventional thresholds, followed by foam (approximately 17%) and surgery (approximately 5%). With regard to secondary outcomes, health gains at 6 weeks (p < 0.005) were greater for EVLA than for foam (EQ-5D, p = 0.004). There were fewer procedural complications in the EVLA group (1%) than after foam (7%) and surgery (8%) (p < 0.001). Participants returned to a wide range of behaviors more quickly following foam or EVLA than following surgery (p < 0.05). There were no differences in VCSS between the 3 treatments. Truncal ablation rates were higher for surgery (p < 0.001) and EVLA (p <
than for foam, and were similar for surgery and EVLA. The authors concluded that considerations of both the 6-month clinical outcomes and the estimated 5-year cost-effectiveness suggested that EVLA should be considered as the treatment of choice for suitable patients.

Marsden et al (2015) investigated the cost-effectiveness of interventional treatment for VV in the United Kingdom National Health Service (UK NHS), and informed the national clinical guideline on VV, published by the National Institute of Health and Care Excellence (NICE). An economic analysis was constructed to compare the cost-effectiveness of surgery, endo-thermal ablation (ETA), ultrasound-guided foam sclerotherapy (UGFS), and compression stockings (CS). The analysis was based on a Markov decision model, which was developed in consultation with members of the NICE guideline development group (GDG). The model had a 5-year time horizon, and took the perspective of the UK NHS. Clinical inputs were based on a network meta-analysis (NMA), informed by a systematic review of the clinical literature. Outcomes were expressed as costs and quality-adjusted life years (QALYs). All interventional treatments were found to be cost-effective compared with CS at a cost-effectiveness threshold of £20,000 per QALY gained; ETA was found to be the most cost-effective strategy overall, with an incremental cost-effectiveness ratio of £3,161 per QALY gained compared with UGFS. Surgery and CS were dominated by ETA. The authors concluded that interventional treatment for VV is cost-effective in the UK NHS. Specifically, based on current data, ETA is the most cost-effective treatment in people for whom it is suitable. The results of this research were used to inform recommendations within the NICE guideline on VV.

Compression Following Treatment for Varicose Veins:

El-Sheikha et al (2015) stated that consensus regarding compression following treatment of VV has yet to be reached. This systematic review aimed to establish the optimal compression regimen after venous treatment. A systematic review of MEDLINE, Embase and CENTRAL was performed to
identify RCTs investigating different compression strategies following treatment for superficial venous insufficiency. A total of 7 RCTs comparing different durations and methods of compression fulfilled the inclusion criteria. The treatment modality was open surgery in 3 trials, foam sclerotherapy in 2 and EVLA in 2 trials. The quality of the studies was variable, and significant sources of potential bias were present. Both the studies and compression regimens used were heterogeneous; 10 products were used in 6 general regimens for a duration of 0 to 42 days. One study suggested that 7 days rather than 2 days of stockings following EVLA was associated with superior QoL and less pain at 1 week. Another study reported that, following surgery, application of a compression stocking after 3 days of bandaging was associated with a slightly longer recovery than no compression after 3 days. One study recorded compliance clearly, finding it to be only 40%. The quality and heterogeneity of the studies precluded meta-analysis. The authors concluded that there is currently little quality evidence upon which to base any recommendations concerning compression following treatment for VV.

**Micronized Purified Flavonoid Fraction Therapy:**

Pietrzycka and colleagues (2015) stated that the etiology of VV involves various factors and pathomechanisms including endothelial cell activation or dysfunction, venous hypertension, vein wall hypoxia, shear stress disturbances, inflammatory reaction activation or free radical production. To improve the understanding of the mechanisms of potential pharmacological interventions for chronic venous disease, these researchers evaluated the influence of micronized purified flavonoid fraction (MPFF) on the relationship between antioxidant enzyme balance, endothelin-1 (ET-1) and tumor necrosis factor-alpha (TNF-α) levels. Blood samples were obtained from 89 women with primary VV; 34 were treated with MPFF and 55 did not receive any phlebotropic drug treatment. For the evaluation of the blood antioxidant enzyme balance, catalase (CAT) and superoxide dismutase (SOD) activity was assessed and the CAT/SOD ratio was calculated. Patients taking MPFF
had significantly lower ET-1 levels than those not taking MPFF [median (25 to 75th quartile): 24.2 (22.30 to 27.87) versus 37.62 (24.9 to 44.58) pg/ml; p < 0.05]. In those taking MPFF, a higher CAT/SOD ratio [39.8 (24.7 to 72.6) versus 28.8 (16.3 to 57.7); p < 0.05] and a lower TNF-α concentration [6.82 (4.42 to 13.39) versus 12.94 (6.01 to 27.33) pg/ml; p < 0.05] was also observed. In women not taking MPFF, ET-1 levels increased with the CAT/SOD ratio. In those taking MPFF, the ET-1 level was stable at about 25.0 pg/ml; up to a CAT/SOD ratio of 100. TNF-α level increased continuously with an increasing CAT/SOD ratio; however, the highest levels of TNF-α were observed in women not taking MPFF. The authors concluded that they demonstrated the ability of MPFF to effectively lower the levels of ET-1 and TNF-α in patients with chronic venous disease. They stated that further investigations are needed to define the therapeutic potential of MPFF including the potential effect on chronic subclinical inflammation, antioxidant imbalance and vascular dysfunction during the development of chronic venous disease.

Cyanoacrylate Tissue Adhesive (e.g., the VariClose Vein Sealing System and the VenaSeal Closure System):

The VenaSeal Closure System:

The VenaSeal Closure System (Sapheon Inc., Morrisville, NC) is a minimally invasive, non-tumescent, non-thermal and non-sclerosant procedure that uses a medical adhesive to close the diseased vein in patients with symptomatic venous reflux disease. Unlike other treatments, the VenaSeal Closure System does not require tumescent anesthesia, allowing patients to return to their normal activities following the procedure; it also eliminates the risk of nerve or other heat-related injuries associated with thermal-based procedures, and thus may reduce the need for compression stockings post-procedure.

Toonder et al (2014) noted that percutaneous thermo-ablation techniques are still being used today and seem more effective than non-thermal techniques. However, thermal techniques
require anesthesia and potentially may cause inadvertent
damage to surrounding tissues such as nerves. Cyanoacrylate
adhesive has a proven record, but not for the treatment of
chronic venous disease of the leg. Innovation has led to the
development of the VenaSeal Sapheon Closure System, which
has been designed to use a modified cyanoacrylate glue as a
new therapy for truncal vein incompetence. These researchers
examined the feasibility of ultrasound-guided cyanoacrylate
adhesive perforator embolization (CAPE). The authors stated
that results of this feasibility study showed a 76% occlusion
rate of incompetent perforating veins without serious
complications; further investigation with a dedicated delivery
device in a larger patient population is needed.

McHugh and Leahy (2014) stated that endothermal treatment
of the great saphenous vein has become the first line of
treatment for superficial venous reflux. Newer treatments,
especially non-thermal ablation have potential benefits both for
patient acceptability and decreased risk of nerve injury. These
researchers described the current non-thermal options
available including advantages and disadvantages. Ultrasound-
guided foam sclerotherapy avoids the risk of nerve injury,
however it is not as effective as endothermal ablation.
Mechano-chemical endovenous ablation combines mechanical
endothelial damage using a rotating wire, with the infusion of a
liquid sclerosant (the ClariVein System). Reports suggested that
this system is safe and effective, eliminating the need for
tumescent anesthesia with no reported case of nerve injury.
Finally the VenaSeal Closure System comprises the endovenous
delivery of cyanoacrylate tissue adhesive to the vein causing
fibrosis. Peri-operative discomfort seems to be minimal but the
complication of thrombophlebitis has been reported in up to 15
% of patients. The authors concluded that non-thermal options
promise comparable treatment efficacy without the added
morbidity associated with high thermal energies. They stated
that the potential of treating venous reflux without the risk of
nerve damage may change how surgeons approach venous
disease.
On February 20, 2015, the FDA granted pre-market approval of the VenaSeal Closure System to treat superficial varicosities of the legs through endovascular embolization and is intended for adults with clinically symptomatic venous reflux diagnosed by duplex ultrasound. The FDA approval was based on a multi-center, RCT by Morrison et al (2015).

Morrison and colleagues (2015) noted that preliminary evidence suggests that CAPE may be effective in the treatment of incompetent GSVs. These investigators reported early results of a RCT of CAPE versus RFA for the treatment of symptomatic incompetent GSVs. A total of 222 subjects with symptomatic GSV incompetence were randomly assigned to receive either CAPE (n = 108) with the VenaSeal Closure System or RFA (n = 114) with the ClosureFast System. After discharge, subjects returned to the clinic on day 3 and again at months 1 and 3. The study's primary end-point was closure of the target vein at month 3 as assessed by duplex ultrasound and adjudicated by an independent vascular ultrasound core laboratory. Statistical testing focused on showing non-inferiority with a 10 % delta conditionally followed by superiority testing. No adjunctive procedures were allowed until after the month 3 visit, and missing month 3 data were imputed by various methods. Secondary end-points included patient-reported pain during vein treatment and extent of ecchymosis at day 3. Additional assessments included general and disease-specific quality of life surveys and adverse event rates. All subjects received the assigned intervention. By use of the predictive method for imputing missing data, 3-month closure rates were 99 % for CAE and 96 % for RFA. All primary end-point analyses, which used various methods to account for the missing data rate (14 %), showed evidence to support the study's non-inferiority hypothesis (all p < 0.01); some of these analyses supported a trend toward superiority (p = 0.07 in the predictive model). Pain experienced during the procedure was mild and similar between treatment groups (2.2 and 2.4 for CAPE and RFA, respectively, on a 10-point scale; p = 0.11). At day 3, less ecchymosis in the treated region was present after CAPE compared with RFA (p < 0.01). Other adverse events occurred...
at a similar rate between groups and were generally mild and well-tolerated. The authors concluded that CAPE was proven to be non-inferior to RFA for the treatment of incompetent GSVs at month 3 after the procedure. Both treatment methods showed good safety profiles; CAPE does not require tumescent anesthesia and is associated with less post-procedure ecchymosis. While these findings supported non-inferiority, the reliability of this approach is unclear. These early results need to be validated by well-designed studies with lower rates of data loss and longer follow-up.

Furthermore, an UpToDate review on “Overview and management of lower extremity chronic venous disease” (Alguire and Scovell, 2015) does not mention VenaSeal/non-thermal ablation as a therapeutic option.

Proebstle et al (2015) noted that cyanoacrylate (CA) embolization of refluxing GSVs has been previously described. The outcomes from a multi-center study are still lacking. A prospective, multi-center study was conducted in 7 centers in 4 European countries to abolish GSV reflux by endovenous CA embolization. Neither tumescent anesthesia (Ta) nor post-interventional compression stockings were used. Varicose tributaries remained untreated until at least 3 months after the index treatment. Clinical examination, quality of life assessment, and duplex US evaluation were performed at 2 days and after 1, 3, 6, and 12 months. In 70 patients, of whom 68 (97.1%) were available for 12-month follow-up, 70 GSVs were treated. Two-day follow-up showed 1 proximal and 1 distal partial re-canulization; 3 additional proximal re-canulizations were observed at 3-month (n = 2) and 6-month (n = 1) follow-up. Cumulative 12-month survival free from re-canulization was 92.9% (95% CI: 87.0% to 99.1%). Mean (standard deviation) Venous Clinical Severity Score improved from 4.3 ± 2.3 at baseline to 1.1 ± 1.3 at 12 months. Aberdeen Varicose Vein Questionnaire score showed an improvement from 16.3 at baseline to 6.7 at 12 months (p < 0.0001). Side effects were generally mild; a phlebitic reaction occurred in 8 cases (11.4%) with a median duration of 6.5 days (range of 2 to
Pain without a phlebitic reaction was observed in 5 patients (8.6%) for a median duration of 1 day (range of 0 to 12 days). No serious AEs occurred; and paresthesia was not observed. The authors concluded that endovenous CA embolization of refluxing GSVs was safe and effective without the use of TA or compression stockings. Moreover, they stated that further work is needed to compare CA against endothermal ablation in RCTs.

Lam and colleagues (2017) stated that the treatment of incompetent truncal veins has been innovated by the introduction of minimally invasive non-thermal non-tumescent (NTNT) techniques. One of these consists of the use of cyanoacrylate glue to occlude the vein lumen by means of the VenaSeal device. These investigators evaluated NTNT ablation of incompetent saphenous trunks using the VenaSeal device. They concluded that cyanoacrylate adhesive embolization of incompetent truncal veins using the VenaSeal device is a safe and effective innovative technique. Moreover, they stated that further studies are needed to evaluate anatomical and clinical outcomes at long-term.

Morrison et al (2017) noted that endovenous CA closure (CAC) is a new FDA-approved therapy for treatment of clinically symptomatic venous reflux in saphenous veins. The device is indicated for the permanent closure of lower extremity superficial truncal veins, such as the GSV. Early results from a randomized trial of CAC have been reported previously. These investigators reported 1-year outcomes. There were 222 subjects with symptomatic GSV incompetence randomly assigned to receive either CAC (n = 108) or RFA (n = 114). After the month 3 visit, subjects could receive adjunctive therapies aimed at treating visible varicosities and incompetent tributaries. Vein closure was assessed at day 3 and months 1, 3, 6, and 12 using duplex US. Additional study visit assessments included the Venous Clinical Severity Score; Clinical, Etiology, Anatomy, and Pathophysiology classification; EuroQol-5 Dimension; and Aberdeen Varicose Vein Questionnaire. Both time to closure and time to first re-opening of the target vein
were evaluated using survival curve analysis; AEs were evaluated at each visit. Of 222 enrolled and randomized subjects, a 12-month follow-up was obtained for 192 (95 CAC and 97 RFA; total follow-up rate, 192/222 [86.5 %]). By month 1, 100 % of CAC subjects and 87 % of RFA subjects demonstrated complete occlusion of the target vein. By month 12, the complete occlusion rate was nearly identical in both groups (97.2 % in the CAC group and 97.0 % in the RFA group); 12-month freedom from re-occlusion was similar in the CAC and RFA groups, although there was a trend toward greater freedom from re-occlusion in the CAC group (p = 0.08). Symptoms and quality of life improved equally in both groups. Most AEs were mild-to-moderate and not related to the device or procedure. The authors concluded that in patients with incompetent GSVs, treatment with both CAC and RFA resulted in high occlusion rates. Time to complete occlusion was faster with CAC, and freedom from re-opening was higher after CAC; quality of life scores improved equally with both therapies.

This study had several drawbacks: (i) this trial included a modest drop-out rate, with month 12 data unavailable for 13 of 108 (12.0 %) subjects in the CAC group (9 withdrawn and 4 visits not done) and 19 of 114 (16.6 %) subjects in the RFA group (8 withdrawn and 11 visits not done), (ii) blinding, although potentially advantageous, was not feasible because RFA requires TA administration, and CAC has characteristic findings on ultrasound. However, the primary study outcome (anatomic closure) was easily judged with ultrasound and is objective, (iii) ultrasound interpretations performed by study investigators could have introduced bias; however, the core laboratory had no knowledge of the sites’ findings at the time of the readings, and their findings agreed with those of the investigators (there was 100 % agreement between investigator reads and core laboratory reads; k statistic was 1.0), and (iv) to minimize confounding due to non-device-related post-intervention factors, subjects in both groups were asked to use compression stockings after the index procedure for 7 days. This was done solely for the trial, but it was not done for 2 prior studies of CAC. Whether compression stockings improve
complete occlusion rates could be the subject of further study.

In a prospective, single-arm, single-center, feasibility study, Almeida et al (2017) evaluated the long-term safety and effectiveness of endovenous cyanoacrylate (CA)-based closure of incompetent GSV. This trial was conducted at the Canela Clinic (La Romana, Dominican Republic) to assess the effectiveness and safety of a CA-based adhesive for GSV closure at 36 months after treatment. A total of 38 subjects were treated by injection of small boluses of CA under US guidance and without the use of peri-venous TA or post-procedure graduated compression stockings. Periodic scheduled follow-up was performed during 36 months. At month 36, there were 29 subjects who were available for follow-up. Complete occlusion of the treated veins was confirmed by duplex US in all subjects with the exception of 2 subjects showing re-canalization at month 1 and month 3. Kaplan-Meier analysis revealed an occlusion rate at month 36 of 94.7 % (95 % CI: 87.9 % to 100 %). The mean Venous Clinical Severity Score (VCSS) improved from 6.1 ± 2.7 at baseline to 2.2 ± 0.4 at month 36 (p < 0.0001). Pain, edema, and varicosities (VCSS subdomains) improved in 75.9 %, 62.1 %, and 41.4 % of subjects, respectively, at month 36. Overall AEs were mild or moderate and self-limited. The authors concluded that CA adhesive appeared to be an effective and safe treatment for saphenous vein closure, with long-term occlusion rates comparable to those of other thermal and non-thermal methods and with no reported serious AEs. This was a small study (n = 38) with a rather high drop-out rate (23.7 %; 9 out of 38).

Gibson and Ferris (2017) noted that CA closure of the GSV with the VenaSeal Closure System is a relatively new modality. Studies have been limited to moderate-sized GSV and some have mandated post-operative compression stockings. These investigators reported the results of a prospective study of CA closure for the treatment of GSV, SSV, and/or accessory saphenous veins (ASV) up to 20 mm in diameter. A total of 50 subjects with symptomatic GSV, SSV, and/or ASV incompetence were each treated at a single session. Compression stockings
were not used post-procedure. Subjects returned to clinic at week 1 and again at 1 month. Post-procedure evaluations were performed at 7 days and 1 month and included numerical pain rating score, revised venous clinical severity score, the Aberdeen Varicose Vein Questionnaire score, and time to return to work and normal activities. Duplex US was performed at each visit. Procedural pain was mild (numerical pain rating scale 2.2 ± 1.8). All treated veins (48 GSV vein, 14 ASV, and 8 SSV) had complete closure by duplex US at 7 days and 1 month. Mean time to return to work and normal activities was 0.2 ± 1.1 and 2.4 ± 4.1 days, respectively. The revised venous clinical severity score was improved to 1.8 ± 1.4 (p < 0.001) and Aberdeen Varicose Vein Questionnaire score to 8.9 ± 6.6 (p < 0.001) at 1 month. Phlebitis in the treatment area or side branches occurred in 10 subjects (20%) and completely resolved in all but 1 subject (2%) by 1 month; 98% of subjects were "completely" or "somewhat" satisfied, and 2% "unsatisfied" with the procedure at 1 month, despite the protocol disallowance of concomitant side branch treatment. The authors concluded that CA closure was safe and effective for the treatment of 1 or more incompetent saphenous or accessory saphenous veins. Closure rates were high even in the absence of the use of compression stockings or side branch treatment. Time back to work or normal activities was short and improvements in venous severity scores and QOL were significant, comparing favorably with alternative treatment methods.

The drawbacks of this study included: (i) its single-arm design, (ii) relatively small sample size (n = 50) at a single center, (iii) some end-points may be biased positively or negatively by the absence of a concurrent comparator group, and both the patients and physicians were aware that CA closure is a relatively novel procedure, and (iv) the short-term follow-up (1 month).

The VariClose Vein Sealing System:

Bozkurt and Yilmaz (2016) stated that cyanoacrylate ablation is
the newest non-thermal vein ablation technique. In a prospective comparative study, these investigators presented the 1-year results of a new cyanoacrylate glue versus endovenous laser ablation for the treatment of venous insufficiency. A total of 310 adult subjects were treated with cyanoacrylate ablation or endovenous laser ablation. The primary end-point of this study was complete occlusion of the great saphenous vein; secondary end-points were procedure time, procedural pain, ecchymosis at day 3, adverse events (AEs), changes from baseline in VCSS, and AVVQ. Operative time was shorter (15 ± 2.5 versus 33.2 ± 5.7, p < 0.001), and peri-procedural pain was less (3.1 ± 1.6 versus 6.5 ± 2.3, p < 0.001) in cyanoacrylate ablation group compared to the endovenous laser ablation group. Ecchymosis on the 3rd day was also significantly less in cyanoacrylate ablation group (p < 0.001). Temporary or permanent paresthesia developed in 7 patients in endovenous laser ablation group and none in cyanoacrylate ablation group (p = 0.015). Closure rates at 1, 3, and 12 months were 87.1, 91.7, and 92.2 % for endovenous laser ablation and 96.7, 96.6, and 95.8 % for cyanoacrylate ablation groups, respectively. Closure rate at 1st month was significantly better in cyanoacrylate ablation group (p < 0.001). Although there was a trend of better closure rates in cyanoacrylate ablation patients, this difference did not reach to the statistical difference at 6th and 12th month (p = 0.127 and 0.138, respectively). Both groups had significant improvement in VCSS and AVVQ post-operatively (p < 0.001), but there was no significant difference in VCSS and AVVQ scores between the groups at 1st, 6th, and 12 months. Only a slightly better well-being trend was noted in cyanoacrylate ablation group in terms of AVVQ scores (p = 0.062). The authors concluded that the safety and effectiveness analysis showed that cyanoacrylate ablation is a safe, simple method that can be recommended as an effective endovenous ablation technique. Moreover, they stated that the follow-up data more than 1 year will clarify the future role of cyanoacrylate ablation for the treatment incompetent great saphenous veins.

Tekin and colleagues (2016) noted that endothermal treatment
of the great saphenous vein has become the 1st line of
treatment for superficial venous reflux. A new technique for
venous insufficiency is non-thermal ablation with vein sealing
system that comprises the endovenous delivery of
cyanoacrylate tissue adhesive to the vein causing fibrosis. In a
single-center, prospective study, these researchers examined
the effectiveness of treatment of great saphenous vein
incompetence in 62 patients with vein sealing system
(VariClose). All cases were implemented under local
anesthesia. Tumescent anesthesia was not required. Patients
were not given any NSAID post-operatively; advised to wear
elastic bandages for 1 day; and compression stockings were not
offered. Treatment success was defined as complete occlusion
of treated vein or re-canalized segment shorter than 5 cm.
Subtotal re-canalization was defined as great saphenous vein
flow containing 5 to 10 cm segment of treated vein. A re-
canalized great saphenous vein or treatment failure was
defined as an open part of the treated vein segment more than
10 cm in length. At 1 week and 1 month control, duplex scans
showed total occlusion for all patients (100 %), total occlusion
for 58 patients (93.5 %), and subtotal occlusion for 4 patients
(6.5 %) at 3rd month. At the end of 6 months, total occlusion
56 patients (90.3 %) and subtotal occlusion for 2 patients (3.2 %).
For 4 (6.5 %) patients, no occlusion was observed, and the
diameter was greater than 11 mm. Embolization of great
saphenous vein with cyanoacrylate has been performed since
the beginning of this decade. Combined chemical and physical
mechanism of action resulted in permanent vein closure. In a
recently published study, a 24-month occlusion rate of 92 %
was demonstrated. The most commonly reported
complications of cyanoacrylate use for the treatment of
varicose vein disease, so far, include ecchymosis and phlebitis.
Almeida et al. reported that phlebitis is the most frequent side
effect at a rate of 16 %. In this study, phlebitis rate was not as
high as reported. It may be caused due to shorter time of
follow-up in the hospital. The authors concluded that
endovenous ablation of incompetent great saphenous vein with
cyanoacrylate-based glue is feasible. Operation time is short,
and tumescent anesthesia is unnecessary as post-procedure
compression stockings; lack of significant side effects and an yearly success rate of 100 % are benefits of the system. These findings need to be validated by well-designed studies with larger sample size and longer follow-up.

In a retrospective study, Yasim and associates (2017) presented the early results of the use of N-butyl cyanoacrylate (VariClose)-based non-tumescent endovenous ablation for the treatment of patients with varicose veins. A total of 180 patients with varicose veins due to incompetent saphenous veins were treated with the VariClose endovenous ablation method between May 2014 and November 2014. Participants consisted of 86 men and 94 women, with a mean age of 47.7 ± 11.7 years; they had a great saphenous vein diameter greater than 5.5 mm and a small saphenous vein diameter greater than 4 mm in conjunction with reflux for more than 0.5 s. Patients with varicose veins were evaluated with venous duplex examination, CEAP, and their VCSS were recorded. The median CEAP score of patients was 3, and the saphenous vein diameters were between 5.5 and 14 mm (mean of 7.7 ± 2.1 mm). A percutaneous entry was made under local anesthesia to the great saphenous vein in 169 patients and to the small saphenous vein in 11 patients. Duplex examination immediately after the procedure showed closure of the treated vein in 100 % of the treated segment. No complications were observed. The mean follow-up time was 5.5 months (ranging from 3 to 7). Re-canalization was not observed in any of the patients during follow-up. The average VCSS was 10.2 before the procedure and decreased to 3.9 after 3 months (p < 0.001). The authors concluded that the application of N-butyl cyanoacrylate (VariClose) is an effective method for treating varicose veins; it yielded a high endovenous closure rate, with no need for tumescent anesthesia. However, long-term results are currently unknown.

Furthermore, Bootun and colleagues (2016b) stated that the early results of 2 recently launched non-thermal, non-tumescent methods, mechanochemical endovenous ablation (MOCA) and cyanoacrylate glue, are promising.
Koramaz and associates (2017) retrospectively compared an n-butyl cyanoacrylate (NBCA)-based ablation method with EVLA for the management of incompetent GSV. Between May 2013 and August 2014, there were 339 patients with incompetent varicose veins who were treated with either the endovenous application of NBCA (VariClose Vein Sealing System [VVSS]; Biolas, Ankara, Turkey) or EVLA. The pre-procedural, intra-procedural, post-procedural, and follow-up data of the patients were collected and retrospectively compared. The mean age was 45.09 ± 12 years in the VVSS group and 47.08 ± 11 years in the EVLA group (p = 0.113). The average ablated vein length was 31.97 ± 6.83 cm in the VVSS group and 31.65 ± 6.25 cm in the EVLA group (p = 0.97). The average tumescent anesthesia use was 300 ml (range of 60 to 600 ml) in the EVLA group. The average procedure time was 7 minutes (range of 4 to 11 minutes) in the VVSS group and 18 minutes (range of 14 to 25 minutes) in the EVLA group (p < 0.01). On the basis of US examinations performed at the end of the procedure, all procedures in both groups were successful, and the target vein segments were fully occluded. The 12-month total occlusion rates in the VVSS and EVLA groups were 98.6% and 97.3%, respectively (p = 0.65). In both the VVSS and EVLA groups, the VCSS declined significantly with no difference between groups. There were fewer AEs after VVSS treatment compared with EVLA treatment (pigmentation, p ≤ 0.002; phlebitis, p ≤ 0.015). There was no need for tumescent anesthesia in the VVSS group. The authors concluded that the NBCA-based vein sealing system was a fast and effective therapeutic option for the management of incompetent saphenous veins that did not involve tumescent anesthesia, compression stockings, paresthesia, burn marks, or pigmentation. Moreover, they stated that further large-scale studies with long-term outcomes are needed to identify the optimal treatment modalities for patients with SVI.

Vos and co-workers (2017) performed a systematic review and meta-analysis to evaluate the effectiveness of MOCA and cyanoacrylate vein ablation (CAVA) for GSV incompetence.
Medline, Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane databases were searched for papers published between January 1966 and December 2016. Eligible articles were prospective studies that included patients treated for GSV incompetence and described the primary outcome. Exclusion criteria were full text not available, case reports, retrospective studies, small series (n less than 10), reviews, abstracts, animal studies, studies of SSV incompetence, and recurrent GSV incompetence. Primary outcome was anatomic success; secondary outcomes were initial technical success, VCSS, AVVQ score, and complications. A total of 15 articles met the inclusion criteria. Pooled anatomic success for MOCA and CAVA was 94.7% and 94.8% at 6 months and 94.1% and 89.0% at 1 year, respectively; VCSS and AVVQ score significantly improved after treatment with MOCA and CAVA. The authors concluded that these findings were promising for these novel techniques that could serve as alternatives for thermal ablation techniques. However, they stated that to determine their exact role in clinical practice, high-quality RCTs comparing these novel modalities with well-established techniques are needed.

Eroglu and colleagues (2017) presented mid-term results of patients with varicose veins treated with N-butyl cyanoacrylate (VariClose), a non-tumescent endovenous ablation technique. Endovenous ablation was performed on 180 patients with saphenous vein incompetence between May and October 2014. A total of 168 subjects capable of being followed-up for 30 months were included. Patients' pre- and post-operative data were recorded. Procedures were performed on the GSV in 159 patients and on the SSV in 9 patients. Saphenous vein diameters ranged between 5.5 mm and 14 mm. Full ablation was achieved in all patients following the procedure. No complications were encountered. Patients were monitored for 30 months. Ablation rates were 100% at the 3rd month, 98.3% at the 6th month, 96.6% at 1 year, and 94.1% at 30 months. Mean VCSS was 10.2 before procedures, decreasing to 3.9 at 3 months, 4.2 at 6 months, 2.9 at 12 months, and 2.7 at 30 months (p = 0.000). The authors concluded that due to its high
success rate, absence of complications, no tumescent anesthesia requirement and high patient satisfaction, endovenous ablation with N-butyl cyanoacrylate is a good method. However, they stated that long-term follow-up results are needed.

Prasad and associates (2017) noted that recurrent lower limb venous insufficiency is often a challenge in clinical practice and is most commonly due to incompetent perforators. Many of these patients do not have adequate symptom relief with compression and require some form of treatment for incompetent perforator interruption. Various methods have been tried with different efficiencies. These investigators evaluated the feasibility, safety and effectiveness of an outpatient combined cyanoacrylate adhesion-sodium tetradecyl sulphate sclerotherapy for the treatment of patients with symptoms of persistent or recurrent lower limb venous insufficiency secondary to incompetent perforators. A total of 83 limbs of 69 patients with symptoms of persistent or recurrent lower limb venous insufficiency secondary to incompetent perforators were treated with cyanoacrylate embolization of incompetent perforators and sclerotherapy of dilated collateral veins (surface branch varicose veins). Technical success, procedural pain, perforator occlusion, venous occlusion, clinical improvement and ulcer healing were assessed. Follow-up was done 3- and 6-month post-procedure. Procedure could be successfully performed in all patients; a total of 191 perforators were treated. Perforator and varicose veins occlusion rate was 100 %. Deep venous extension of cyanoacrylate occurred in 4 (4.8 %) patients, with no adverse clinical outcome. Venous clinical severity score improved from a baseline of 8.18 ± 3.60 to 4.30 ± 2.48 on 3-month follow-up and 2.42 ± 1.52 on 6-month follow-up (p < 0.0001). All ulcers showed complete healing within 3 months. Significant prolonged thrombophlebitis occurred in 38.5 % of limbs. The authors concluded that combined cyanoacrylate adhesion and sodium tetradecyl sulphate sclerotherapy was technically easy, had a lot of advantages including being an out-patient procedure and highly effective but with a guarded safety
profile. The main drawbacks of this study were its relatively small sample size ($n = 69$) and short-term follow-up (6 months); and the findings were confounded by the combined use of cyanoacrylate adhesion and sodium tetradecyl sulphate sclerotherapy.

**ClariVein:**

Witte et al (2015) noted that endovenous mechano-chemical occlusion using the ClariVein catheter is a new technique combining mechanical injury to the venous endothelium coupled with simultaneous catheter-guided infusion of a liquid sclerosant. This produces irreversible damage to the endothelium resulting in fibrosis of the vein. The technique is related to a low complication rate and a success rate of 96% at 2 years and sustained quality of life improvement. This closure rate is comparable to endothermal techniques, but significantly less post-operative pain and earlier return to normal activities and work has been reported with endovenous mechano-chemical occlusion. The authors concluded that mechano-chemical occlusion using ClariVein has proven to be safe and effective and has several advantages compared to endothermal techniques. The possibility of retrograde ablation of distal SSV insufficiency in C6 ulceration is considered a significant advantage. Moreover, they stated that randomized comparative studies with long-term follow-up will continue to define the definite place of mechano-chemical occlusion.

Deijen et al (2016) stated that mechano-chemical endovenous ablation is a novel technique for the treatment of GSV and SSV incompetence which combines mechanical injury of the endothelium with simultaneous infusion of liquid sclerosant. The main objective of this study was to evaluate early occlusion. All consecutive patients who were eligible for the treatment with mechano-chemical endovenous ablation were included. Inclusion period was from the introduction of the device in the hospitals (September 2011 and December 2011) until December 2012. A total of 449 patients were included representing 570 incompetent veins. In 506 treated veins,
duplex ultrasonography was performed at follow-up: 457 veins (90 %) were occluded at a follow-up of 6 to 12 weeks. In univariate and multivariate analysis, failure of treated GSV was associated with sapheno-femoral junction incompetence (OR 4; 95 % CI: 1.0 to 17.1, p = 0.049). The authors concluded that the ClariVein device appeared to be safe and had a high short-term technical effectiveness. Long-term clinical outcomes are needed to ascertain the clinical value of the ClariVein.

In a RCT, Lam et al (2016) identified the ideal polidocanol dosage and form for mechano-chemical ablation in order to occlude the GSV. When adhering to safe dosage levels, sclerosants with higher concentrations potentially limit the extent of treatment. It has been demonstrated that this problem may be overcome by using polidocanol as a microfoam. This paper was established on findings of a preliminary analysis. The initial study was a single-blinded multi-center RCT where patients are allocated to 3 treatment arms. Group 1 consisted of mechano-chemical ablation + 2 % polidocanol liquid, group 2: mechano-chemical ablation + 3 % polidocanol liquid, and group 3: mechano-chemical ablation + 1 % polidocanol foam. A total of 87 (34 males and 53 females (60.9 %)), mean age of 55 years; S.D. 16.0 (range of 24 to 84), were enrolled in the study. Treatment length was 30 cm (range of 10 to 30) for 95.2 % of the patients. Mean operating time was 16 minutes (range of 5 to 70). The mean sapheno-femoral junction diameter (7.7 mm) was similar in all 3 groups. At 6 weeks post-treatment duplex ultrasound showed that 25 out of 25 (100 %), 27 out of 28 (96.4 %) and 13 out of 23 (56.5 %) were occluded in the mechano-chemical ablation + 2 % polidocanol liquid, mechano-chemical ablation + 3 % polidocanol liquid and mechano-chemical ablation + 1 % polidocanol microfoam respectively (p < 0.001). However, stricter scrutiny showed that the anatomical success rate defined as occlusion of at least 85 % of the treated length to be 88.0 %, 85.7 % and 30.4 % respectively (p < 0.001). The authors concluded that mechano-chemical ablation using ClariVein combined with 1 % polidocanol microfoam is significantly less effective and should not be considered as a treatment option of incompetent truncal
veins. They stated that further investigation to determine the ideal polidocanol liquid dosage with mechano-chemical ablation is advocated and is being conducted accordingly.

Vun and colleagues (2015) evaluated the effectiveness of the ClariVein system of MOCA of superficial vein incompetence. ClariVein treatment uses a micro-puncture technique and a 4-Fr sheath to allow a catheter to be placed 1.5 cm from the SFJ. Unlike EVLT or RFA, no tumescence is required. The technique depends on a wire rotating at 3,500 r/min causing endothelial damage while liquid sclerosant (1.5 % sodium tetradecyl sulphate) is infused. The wire is pulled back while continuously infusing sclerosant along the target vessel's length. Initially, 8 ml of dilute sclerosant was used, but this was subsequently increased to 12 ml. No routine post-op analgesia was prescribed and specifically no NSAIDs. Procedure times and pain scores (visual analog scale [VAS]) were recorded and compared to EVLT and RFA. All patients were invited for duplex post-procedure. A total of 51 GSV and 6 SSV were treated and followed-up with duplex in the 10 months from July 2011. No major complications or deep vein thrombosis were reported. Duplex showed patency of 3 treated veins with 2 more veins having only a short length of occlusion, giving a technical success rate of 91%. Comparison with 50 RFA and 40 EVLT showed procedure times were significantly less for ClariVein (23.0 ± 8.3 mins) than for either RFA (37.9 ± 8.3 mins) or EVLT (44.1 ± 11.4 mins). Median pain scores were significantly lower for ClariVein than RFA and EVLT (1 versus 5 versus 6, p < 0.01). The authors concluded that MOCA with the ClariVein system is safe and effective. After some initial failures, the use of 12 ml of dilute sclerosant resulted in a very high technical success rate greater than 90% which accorded with the limited published literature; and procedure times and pain scores were significantly better than for RFA and EVLT. These researchers stated that they await the long-term clinical outcomes.

Bootun and associates (2016a) noted that endovenous techniques are, at present, the recommended choice for truncal vein treatment. However, the thermal techniques require
tumescent anesthesia, which can be uncomfortable during administration. Non-tumescent, non-thermal techniques would, therefore, have potential benefits. In a RCT, these investigators compared the degree of pain that patients experience while receiving MOCA or RFA. The early results of this RCT were reported here. Patients attending for the treatment of primary varicose veins were randomized to receive MOCA (ClariVein) or RFA (Covidien Venefit). The most symptomatic limb was randomized. The primary outcome measure was intra-procedural pain using a validated VAS. The secondary outcome measures were change in quality of life and clinical scores, time to return to normal activities and work as well as the occlusion rate. A total of 119 patients were randomized (60 in the MOCA group). Baseline characteristics were similar. Maximum pain score was significantly lower in the MOCA group (19.3 mm, SD ± 19 mm) compared to the RFA group (34.5 mm ± 23 mm; p < 0.001). Average VAS was also significantly lower in the MOCA group (13.4 mm ± 16 mm) compared to the RFA (24.4 mm ± 18 mm; p = 0.001); 66 % attended follow-up at 1 month, and the complete or proximal occlusion rates were 92 % for both groups. At 1 month, the clinical and quality of life scores for both groups had similar improvements. The authors concluded that early results showed that MOCA is less painful than the RFA procedure, and clinical as well as quality of life scores were similarly improved at 1 month. The long-term data including occlusion rates at 6 months and quality of life scores are being collected. Furthermore, Bootun and colleagues (2016b) stated that the early results of 2 recently launched non-thermal, non-tumescent methods, MOCA and cyanoacrylate glue, are promising.

Lam and colleagues (2016) noted that the ClariVein system is an endovenous technique that uses MOCA to treat incompetent truncal veins. This study was conducted to identify the ideal Polidocanol dosage and form for MOCA in order to occlude the GSV. When adhering to safe dosage levels, sclerosants with higher concentrations potentially limit the extent of treatment. It has been demonstrated that this problem may be overcome.
by using Polidocanol as a microfoam. This paper was established on findings of a preliminary analysis. The initial study was a single-blinded, multi-center RCT where patients were allocated to 3 treatment arms: (i) group 1 consisted of MOCA + 2 % Polidocanol liquid, (ii) group 2: consisted of MOCA + 3 % Polidocanol liquid, and (iii) group 3: consisted of MOCA + 1 % Polidocanol foam. A total of 87 patients (34 males and 53 females, mean age of 55 years [SD 16.0 and range of 24 to 84]) were enrolled in the study. Treatment length was 30 cm (range of 10 to 30) for 95.2 % of the patients. Mean operating time was 16 minutes (range of 5 to 70). The mean SFJ diameter (7.7 mm) was similar in all 3 groups. At 6 weeks post-treatment duplex ultrasound showed that 25 out of 25 (100 %), 27 out of 28 (96.4 %) and 13 out of 23 (56.5 %) were occluded in the MOCA + 2 % Polidocanol liquid, MOCA + 3 % Polidocanol liquid, and MOCA + 1 % Polidocanol microfoam respectively (p < 0.001). However, stricter scrutiny showed that the anatomical success rate defined as occlusion of at least 85 % of the treated length to be 88.0 %, 85.7 % and 30.4 % respectively (p < 0.001). The authors concluded that MOCA using ClariVein combined with 1 % Polidocanol microfoam was significantly less effective and should not be considered as a therapeutic option of incompetent truncal veins. They stated that further investigation to determine the ideal Polidocanol liquid dosage with MOCA is advocated and is being conducted accordingly.

Leung and colleagues (2016) stated that endovenous thermal techniques, such as EVLA, are the recommended treatment for truncal varicose veins. However, a disadvantage of thermal techniques is that it requires the administration of tumescent anesthesia, which can be uncomfortable. Non-thermal, non-tumescent techniques, such as MOCA have potential benefits; MOCA combines physical damage to endothelium using a rotating wire, with the infusion of a liquid sclerosant. Preliminary experiences with MOCA showed good results and less post-procedural pain. The Laser Ablation versus Mechanochemical Ablation (LAMA) trial is a single-center RCT in which 140 patients will be randomly allocated to EVLA or MOCA. All patients with primary truncal superficial venous insufficiency (SVI) who meet the eligibility criteria will be invited
to participate in this trial. The primary outcomes are intra-procedural pain and technical efficacy at 1 year, defined as complete occlusion of target vein segment and assessed using duplex ultrasound. Secondary outcomes are post-procedural pain, analgesia use, procedure time, clinical severity, generic and disease-specific quality of life, bruising, complications, satisfaction, cosmesis, time taken to return to daily activities and/or work, and cost-effectiveness analysis following EVLA or MOCA. Both groups will be evaluated on an intention-to-treat basis. The aim of the LAMA trial is to establish whether MOCA is superior to the current first-line treatment, EVLA. The 2 main hypotheses are: (i) MOCA may cause less initial pain and disability allowing a more acceptable treatment with an enhanced recovery, and (ii) this may come at a cost of decreased efficacy, which may lead to increased recurrence and affect longer term quality of life, increasing the requirement for secondary procedures.

In a large, single-center study, Tang and co-workers (2017) examined the effectiveness and patient experience of the ClariVein® endovenous occlusion catheter for varicose veins. A total of 300 patients (371 legs) underwent ClariVein treatment for their varicose veins; 184 for GSV incompetence, 62 bilateral GSV, 23 SSV, 6 bilateral SSV and 25 combined unilateral GSV and SSV. Patients were reviewed at an interval of 2 months post-procedure and underwent Duplex ultrasound assessment. Post-operative complications were recorded along with patient satisfaction. All 393 procedures were completed successfully under local anesthetic. Complete occlusion of the treated vein was initially achieved in all the patients, but at 8 weeks' follow-up, there was only partial obliteration in 13/393 (3.3 %) veins. These were all successfully treated with ultrasound-guided foam sclerotherapy. Procedures were well-tolerated with a mean pain score of 0.8 (0 to 10), and no significant complications were reported. The authors concluded that ClariVein can be used to ablate long and short saphenous varicose veins on a walk-in-walk-out basis. Bilateral procedures can be successfully performed, and these were well-tolerated as can multiple veins in the same leg. They stated that early
results are promising but further evaluation and longer term follow-up are needed.

Witte and colleagues (2016) reported the midterm results of mechanochemical ablation (MOCA) for treating GSV insufficiency. In a 1-year period, 85 consecutive patients (median age of 51.4 years; 71 women) undergoing MOCA with polidocanol in 104 limbs were enrolled in a prospective registry. Patients were evaluated at baseline and during follow-up (4 weeks and 1, 2, and 3 years) using duplex ultrasound, the CEAP (clinical, etiologic, anatomic and pathophysiologic) classification, the Venous Clinical Severity Score (VCSS), the RAND Short Form 36-Item Health Survey (RAND-SF36), and the Aberdeen Varicose Vein Questionnaire (AVVQ). Primary outcome measures were clinical and anatomic success; secondary outcome measures included general and disease-specific quality of life and re-interventions. Technical success (99%) was achieved in all but 1 patient in whom technical problems with the device led to conversion to another method for treatment of 2 limbs. After a median follow-up of 36 months (interquartile range [IQR] 12.5, 46.3), re-canalization occurred in 15 (15%) of 102 successfully treated vein segments. Anatomic success was 92%, 90%, and 87% after 1, 2, and 3 years, respectively. The VCSS improved at all time-intervals compared to the pre-procedure median. The clinical success at 3 years was 83%. The AVVQ and RAND-SF36 scores showed an improvement at all time-intervals compared to baseline values. Between 12 and 36 months, however, a significant deterioration was observed in VCSS, which was accompanied by worsening of disease-specific and general quality of life. The authors concluded that in the longest follow-up of MOCA to-date, this study showed MOCA to be an effective treatment modality for GSV insufficiency at midterm follow-up, but clinical results appeared to drop over time. The major drawbacks of this study were: (i) the results were affected by the chosen definitions of success. Although the definition used is in accordance with previous landmark trials, heterogeneity in the definition among studies was a major problem in comparing results and emphasized the need for standardization of
outcome measures, and (ii) follow-up was not completed for every patient, and questionnaires were not always complete.

Lane and associates (2017) noted that endovenous thermal ablation has revolutionized varicose vein treatment. New non-thermal techniques such as MOCA allow treatment of entire trunks with single anesthetic injections. Previous non-randomized work has shown reduced pain post-operatively with MOCA. This study presented a multi-center, RCT assessing the difference in pain during truncal ablation using MOCA and radiofrequency endovenous ablation (RFA) with 6 months' follow-up. Patients undergoing local anesthetic endovenous ablation for primary varicose veins were randomized to either MOCA or RFA. Pain scores using VAS and number scale (0 to 10) during truncal ablation were recorded. Adjunctive procedures were completed subsequently. Pain after phlebectomy was not assessed. Patients were reviewed at 1 and 6 months with clinical scores, quality of life scores and duplex ultrasound assessment of the treated leg. A total of 170 patients were recruited over a 21-month period from 240 screened. Patients in the MOCA group experienced significantly less maximum pain during the procedure by VAS (MOCA median of 15 mm (IQR 7 to 36 mm) versus RFA 34 mm (IQR 16 to 53 mm), p = 0.003) and number scale (MOCA median of 3 (IQR 1 to 5) versus RFA 4 mm (IQR 3 to 6.5), p = 0.002).

“Average” pain scores were also significantly less in the MOCA group; 74 % underwent simultaneous phlebectomy. Occlusion rates, clinical severity scores, disease specific and generic quality of life scores were similar between groups at 1 and 6 months. There were 2 deep vein thromboses, 1 in each group. The authors concluded that pain secondary to truncal ablation was less painful with MOCA than RFA with similar short-term technical, quality of life and safety outcomes. They stated that further work with larger studies and extended follow-up is needed to evaluate the long-term outcomes and recurrence rates.

The authors noted that “This study was limited by lack of treatment blinding for the patients and interventional clinicians.
This was due to the technical differences between devices, i.e., tumescent injections in the RFA group and device vibration in the MOCA group. Follow-up appointments and ultrasound scanning were treatment blind. A further limitation of this study is the lack of long-term follow-up -- only short-term occlusion rates are assessed in this study, with the primary outcome obtained at the time of procedure. Operating time was not recorded in this study; however, all cases were performed in standardized theatre sessions in single slots with one surgeon performing all tasks, and 74% of patients also underwent simultaneous phlebectomy. A major limitation of all tumescentless techniques is how to treat varicosities left after truncal ablation, with level one evidence now supporting combined treatment with phlebectomies. This study was designed and commenced prior to the completion of latest trial, but took into consideration the fact that phlebectomies cause pain, and so pain scores taken after truncal ablation but before any phlebectomies were completed. This, therefore, represents a significant limitation to the outcomes of this trial, as the pain scores reported above do not assess the complete treatment, except for those patients who did not undergo phlebectomy. Also, this study did not assess pain scores after phlebectomy or after the peri-procedural period.

National Institute for Health and Care Excellence’s guideline on “Endovenous mechanochemical ablation for varicose veins” (2016) stated that “Current evidence on the safety and efficacy of endovenous mechanochemical ablation for varicose veins appears adequate to support the use of this procedure provided that standard arrangements are in place for consent, audit and clinical governance. Clinicians are encouraged to collect longer-term follow-up data”.

Elias and Raines (2012) evaluated the safety and efficacy of the ClariVein system that employs mechanochemical ablation (MOCA) of the great saphenous vein (GSV). Patients eligible for ablation of the GSV underwent micro-puncture access with only local anesthesia to insert a 4 or 5 Fr sheath. The ClariVein catheter was placed through the sheath, the wire was extruded,
and the distal tip of the wire positioned 2 cm from the saphenofemoral junction under ultrasound (US) guidance. Catheter wire rotation was then activated for 2 to 3 seconds at approximately 3,500 rpm. With the wire rotating, infusion of the sclerosant was started simultaneously with catheter pullback. The sclerosant used was 1.5% liquid sodium tetradecyl sulphate. A total of 30 GSVs in 29 patients were treated. All patients have reached 6-month follow-up; the average number of post-operative days was 260. No adverse events (AERs) have been reported; the primary closure rate was 96.7%. The authors concluded that MOCA appeared to be safe and efficacious. The ClariVein technique eliminated the need for tumescent anesthesia. The great majority of incompetent GSVs can be treated with this technique. (This was a small study (n= 29) with short-term follow-up (6 months))

In a prospective cohort study, Boersma and associates (2013) evaluated the feasibility, safety and 1-year results of MOCA of small saphenous vein (SSV) insufficiency. A total of 50 consecutive patients were treated for primary SSV insufficiency with MOCA using the ClariVein device and polidocanol. Initial technical success, complications, patient satisfaction and visual analogue scale (VAS) pain score were assessed. Anatomic and clinical success was assessed at 6 weeks and at 1 year. Initial technical success of MOCA was 100%. At the 6-week assessment, all treated veins were occluded. The 1-year follow-up duplex showed anatomic success in 94% (95% confidence interval [CI]; 0.87 to 1). Venous clinical severity score (VCSS) decreased significantly from 3.0 (interquartile range (IQR) 2 to 5) before treatment to 1.0 (IQR 1 to 3, p < 0.001) at 6 weeks and to 1.0 (IQR 1 to 2, p < 0.001) at 1 year. Median procedural VAS score for pain was 2 (IQR 2 to 4). No major complications were observed, especially no nerve injury. The authors concluded that MOCA was a safe, feasible and efficacious technique for treatment of SSV insufficiency. One-year follow-up showed a 94% anatomic success rate and no major complications.

One of the drawbacks of this study was that the maximum
diameter of treated SSVs was 11 mm. The technical and clinical success of MOCA in larger-diameter varicose veins was still unknown. Pain scores during MOCA were very low. Post-procedural pain scores were not measured. The authors stated that further controlled studies are needed to compare pain with other techniques in SSV ablation. Patients on oral anti-coagulants were excluded; thus, these researchers could not provide data on the effect of anti-coagulant therapy on MOCA. In contrast to endothermal therapy, anti-coagulants might influence clot formation and lead to increased re-canalization.

In a prospective, observational, multi-center report, Bishawi and colleagues (2014) evaluated the efficacy of a tumescent-free technique using MOCA in selected patients with lower extremity chronic venous disease. Demographic information, clinical and procedural data were collected on a customized database. The distribution and extent of venous reflux and the closure rate of the treated veins were assessed with duplex US. Pain was evaluated during the procedure and post-operatively using an analog scale. The presence and severity of complications were recorded. Patient improvement was assessed by clinical-etiopathology-anatomy-pathophysiology (CEAP) class and venous clinical severity score (VCSS). There were 126 patients that were included at baseline, 81 % females, with a mean age of 65.5 ± 14 years. The average BMI was 30.5 ± 6. The mean diameter of the great saphenous vein in the upper thigh was 7.3 mm and the mean treatment length was 38 cm. Adjunctive treatment of the varicosities was performed in 11 % of patients during the procedure. Closure rates were 100 % at 1 week, 98 % at 3 months, and 94 % at 6 months. Post-procedure complications included hematoma 1 %, ecchymosis 9 %, and thrombophlebitis 10 %. There were no cases of venous thromboembolism. There was significant improvement in VCSS (p < 0.001) for all time intervals. The authors concluded that MOCA of the saphenous veins had the advantage of endovenous ablation without tumescent anesthesia, making it an almost pain-free procedure. High occlusion rates with significant clinical improvement can be achieved with this method at short-term.
Ozen et al (2014) evaluated the reliability and 2-year results of ClariVein device used in MOCA of GSV. In the authors’ clinic, a total of 63 patients with GSV insufficiency had been treated using ClariVein device and polidocanol for 2 years. Both legs were treated in 10 of these patients. The anatomical and clinic success were assessed by Doppler US 6 months, 1 year, and 2 years later. The implementation success rate of the technique was 98%. The anatomical success was found as 94% at the end of 6 months, 95% at the end of 1 year, and 95% at the end of 2 years. The venous clinic severity score was found as 3.2 (IQR: 2 to 6) after 6 months, 1.2 (IQR: 1 to 3, p < 0.001) after 1 year, and 1.1 (IQR: 1 to 2, p < 0.001) after 2 years. No complications developed in any of the patients. The authors concluded that ClariVein was a simple, reliable, and efficient treatment method for GSV insufficiency. In 2-year follow-up, the anatomical success rate was found as 95%, and no major complications were observed.

Stanisic et al (2016) stated that MOCA of the GSV and the SSV is an alternative to thermal ablation for the treatment of superficial venous reflux. These researchers evaluated the efficacy of MOCA for the treatment of incompetent GSV and SSV. They included 50 patients (60 legs) with incompetent GSV or SSV. Patients were aged 22 to 71 years, with median age of 41 years. Diameters of the saphenous veins treated were 4 to 16 mm, with median diameter 9 mm. Lengths of incompetent segments of the GSVs were 20 to 45 cm, with median length 36 cm. Lengths of incompetent segments of the SSVs were 12 to 25 cm, with median length of 17 cm. These investigators performed venous ablation using the ClariVein device with simultaneous injection of 2% polidocanol in the dose of 0.2 ml/cm of the treated vein. All patients completed 12 months follow-up. In all patients the procedure resulted in complete occlusion of the incompetent segment of the saphenous vein. Additional foam sclerotherapy was needed in 41 legs (68.3%). After 12 months partial or complete re-canalization was revealed in 1 GSV and 3 SSVs. The remaining veins (93.3%) were completely occluded. During the procedure these
researchers observed transient signs of polidocanol toxicity in 2 patients. The authors concluded that MOCA using the ClariVein device was a safe method for ablation of incompetent truncal veins in patients who prefer to be managed quickly, without pain and with satisfactory results after 1 year.

In a 2-year follow-up on the efficacy of MOCA in patients with symptomatic C2 or more advanced chronic venous disease, Kim and co-workers (2017) reported if early efficacy was maintained at 24 months. Patients with reflux in the great saphenous vein involving the sapheno-femoral junction and no previous venous interventions were included. Demographic information, clinical, and procedural data were collected. The occlusion rate of treated veins was assessed with duplex US. Patient clinical improvement was assessed by CEAP class and venous clinical severity score. Of the initial 126 patients, there were 65 patients with 24 month follow-up. Of these 65 patients, 70% were women, with a mean age of 70 ± 14 years and an average BMI of 30.5 ± 6. The mean great saphenous vein diameter in the upper thigh was 7.6 mm and the mean treatment length was 39 cm. Adjunctive treatment of the varicosities was performed in 14% of patients during the procedure. Closure rates were 100% at 1 week, 98% at 3 months, 95% at 12 months, and 92% at 24 months. There was 1 patient with complete and 4 with partial re-canulization ranging from 7 to 12 cm (mean length 9 cm). There was significant improvement in CEAP and venous clinical severity score (p < 0.001) for all time intervals. The authors concluded that early high occlusion rate with MOCA was associated with significant clinical improvement which was maintained at 24 months, making it a very good option for the treatment of great saphenous vein incompetence.

Whiteley et al (2017) examined the effects of MOCA using ClariVein on ex-vivo GSV with histology and immunofluorescent staining. Extra-fascial GSVs were harvested during surgery for varicose veins and were treated ex-vivo for 10 to 11 minutes with either liquid sclerotherapy or the use of ClariVein, with and without 3% sodium tetradecyl sulfate. Veins were
sectioned and subjected to hematoxylin and eosin staining and immunofluorescent staining for endothelial and smooth muscle cell markers (CD31 and α-actin) to assess overall damage and cell death in the vein wall compared with control sections. Histologic observations confirmed intimal damage from ClariVein, as has been previously shown; however, medial damage was also evident, which was not observed in control or liquid sclerotherapy sections. Immunofluorescent staining in the 3 sections studied showed a 42 % decrease in CD31 staining and 27 % mean reduction in α-actin staining up to a depth of 300 µm with liquid sclerotherapy. This cytotoxic effect was significantly enhanced by MOCA with a reduction in CD31 staining just above 60 % and a 46 % mean decrease in α-actin staining noted up to a depth of 300 µm. Far greater reductions in staining compared with sclerotherapy were observed up to a depth of 600 µm. The authors concluded that MOCA using 3 % sodium tetrade cyl sulfate increased the penetration of the sclerosant and its effect into the vein wall and showed superior rates of tissue destruction compared with liquid sclerotherapy alone. In this model, it appeared not solely to damage the endothelium but also to shear the medial layer, creating small lesions into which sclerosant can flow and exert its cytotoxic effect. These investigators stated that short-term follow-up studies of MOCA showed results that were comparable to those of RFA or EVLA. Initial investigations into the short- to medium-term success rates of ClariVein for treating reflux in the GSV reported excellent closure rates that stand above 95 % up to 1 year after the procedure, with the longest follow-up of 2 years showing 92 % closure. Separate analyses also showed significantly less post-operative pain and faster recovery of the patient with MOCA compared with RFA. This showed a considerable advantage over US-guided foam sclerotherapy, which was associated with a high risk of re-canalization and recurrent reflux even as early as 1 year after the procedure. These researchers noted that as time progresses, the medium- and long-term success rates of MOCA will need to be evaluated and compared with existing treatment modalities.

Witte et al (2017) reported the mid-term results of MOCA for
treating GSV insufficiency. In a 1-year period, 85 consecutive patients (median age of 51.4 years; 71 women) undergoing MOCA with polidocanol in 104 limbs were enrolled in a prospective registry. The patients were evaluated at baseline and during follow-up (4 weeks and 1, 2, and 3 years) using duplex US, the CEAP (clinical, etiologic, anatomic and pathophysiologic) classification, the Venous Clinical Severity Score (VCSS), the RAND Short Form 36-Item Health Survey (RAND-SF36), and the Aberdeen Varicose Vein Questionnaire (AVVQ). Primary outcome measures were clinical and anatomic success. Secondary outcome measures included general and disease-specific QOL and re-interventions. Technical success (99%) was achieved in all but 1 patient in whom technical problems with the device led to conversion to another method for treatment of 2 limbs. After a median follow-up of 36 months (IQR 12.5 to 46.3), re-canalization occurred in 15 (15%) of 102 successfully treated vein segments. Anatomic success was 92%, 90%, and 87% after 1, 2, and 3 years, respectively. The VCSS improved at all time intervals compared to the pre-procedure median. The clinical success at 3 years was 83%. The AVVQ and RAND-SF36 scores showed an improvement at all time intervals compared to baseline values. Between 12 and 36 months, however, a significant deterioration was observed in VCSS, which was accompanied by worsening of disease-specific and general QOL. The authors concluded that in the longest follow-up of MOCA to-date, this study showed MOCA to be an effective treatment modality for GSV insufficiency at mid-term follow-up, but clinical results appeared to drop over time. The authors stated that the results of the present study were affected by the chosen definitions of success. Although the definition used was in accord with previous landmark trials, heterogeneity in the definition among studies was a major problem in comparing results and emphasized the need for standardization of outcome measures. Furthermore, follow-up was not completed for every patient, and questionnaires were not always complete.

While a Cochrane review on “Endovenous ablation therapy (laser or radiofrequency) or foam sclerotherapy versus
conventional surgical repair for short saphenous varicose veins” (Paravastu et al, 2016) did not address the use of MOCA, it is interesting to note that the authors stated that “Further RCTs for all comparisons are required with longer follow‐up (at least 5 years). In addition, measurement of outcomes such as recurrence of reflux, time taken to return to work, duration of procedure, pain, etc., and choice of time points during follow‐up should be standardised such that future trials evaluating newer technologies can be compared efficiently”.

**Polymorphism Genotyping of Matrix Metalloproteinases Genes (e.g., MMP1, MMP2, MMP3, and MMP7) as Markers of Predisposition to Varicose Veins:**

Kurzawski and associates (2009) noted that several risk factors for varicose veins have been identified: female gender, combined with obesity and pregnancy, occupations requiring standing for long periods, sedentary lifestyle, history of deep‐vein thrombosis (DVT) and family history. However, no specific gene variants related to a wide prevalence of varicosities in general population have been identified. Extracellular matrix composition, predominantly maintained by matrix metalloproteinases (MMPs), may affect the vein‐wall structure, which may lead to dilation of vessels and cause varicosities. MMP‐1 (tissue collagenase I) and MMP‐3 (stromelysin I) expression was found to be raised in varicose veins compared with normal vessels. Thus, these investigators carried out a study to evaluate a potential association between MMP1 and MMP3 promoter polymorphisms and a risk of varicose veins. Genotyping for the presence of the polymorphisms -1607dupG (rs1799750) in MMP1 and -1171dupA (rs3025058) in the MMP3 promoter region was performed using polymerase chain reaction (PCR) and restriction‐fragment length polymorphism assays in a group of 109 patients diagnosed with varicose veins and 112 healthy controls. The frequencies of the MMP1 and MMP3 alleles (minor allele frequency 0.440 in patients versus 0.451 in the controls for MMP1-1607*G and 0.514 versus 0.469 for MMP3-1171*dupA, respectively) and of genotypes did not differ significantly between patients and controls. The authors
concluded that MMP1-1607dupG and MMP3-1171dupA promoter polymorphisms were not valuable markers of susceptibility for varicose veins.

Shadrina and colleagues (2017) examined the effects of single nucleotide polymorphisms (SNPs) in the promoter regions of MMP genes rs1799750 (-1607dupG) MMP1, rs243865 (C-1306T) MMP2, rs3025058 (-1171dupA) MMP3, and rs11568818 (A-181G) MMP7 on the risk of varicose vein of the lower extremities in ethnical Russians, residents of the Russian Federation. These researchers genotyped 536 patients with this pathology and 273 healthy participants without history of chronic venous disease. Association was examined using logistic regression analysis. None of the studied polymorphisms showed statistically significant association with the risk of varicose veins of the lower extremities. The authors concluded that these findings provided evidence that these polymorphisms are not involved in the pathogenesis of varicose veins and cannot serve as markers of predisposition to this pathology.

**Matrix Metalloproteinases Inhibitors for the Treatment of Varicose Veins:**

Chen and colleagues (2017) noted that the veins of the lower extremity are equipped with efficient wall, contractile vascular smooth muscle (VSM), and competent valves in order to withstand the high venous hydrostatic pressure in the lower limb and allow unidirectional movement of deoxygenated blood toward the heart. The vein wall structure and function are in part regulated by MMPs, which are zinc-dependent endopeptidases that are secreted as inactive pro-MMPs by different cells in the venous wall including fibroblasts, VSM, and leukocytes. Pro-MMPs are activated by other MMPs, proteinases, and other endogenous and exogenous activators. Matrix metalloproteinases degrade various extracellular matrix (ECM) proteins including collagen and elastin, and could affect other cellular processes including endothelium-mediated dilation, VSM cell migration, and proliferation as well as...
modulation of calcium ion (Ca2+) signaling and contraction in VSM. It is believed that increased lower limb venous hydrostatic pressure increases hypoxia-inducible factors and other MMP inducers such as extracellular MMP inducer, leading to increased MMP expression/activity, ECM protein degradation, vein wall relaxation, and venous dilation. Vein wall inflammation and leukocyte infiltration cause additional increases in MMPs, and further vein wall dilation and valve degradation, that could lead to chronic venous disease and VVs, which are often presented as vein wall dilation and tortuosity, incompetent venous valves, and venous reflux. Different regions of VVs show different MMP levels and ECM proteins with atrophic regions showing high MMP levels/activity and little ECM compared to hypertrophic regions with little or inactive MMPs and abundant ECM. Treatment of VVs includes compression stockings, venotonics, sclerotherapy, or surgical removal. However, these approaches do not treat the cause of VVs, and other lines of treatment may be needed. The authors stated that modulation of endogenous tissue inhibitors of metalloproteinases (TIMPs), and exogenous synthetic MMP inhibitors may provide new approaches in the management of VVs.

Appendix

List: Clinical, Etiological, Anatomical and Pathophysiological classification (CEAP) Classification

Clinical Classification

- C0 No visible or palpable signs of venous disease
- C1 Telangiectasias, reticular veins, malleolar flares
- C2 Varicose veins
- C3 Edema without skin changes
- C4 Skin changes ascribed to venous disease (eg, pigmentation, venous eczema, lipodermatosclerosis)
- C4a pigmentation or eczema
- C4b Lipodermatosclerosis or atrophie blanche
- C5 Skin changes as defined above with healed ulceration
- C6 Skin changes as defined above with active ulceration
CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td></td>
<td><strong>CPT codes covered if selection criteria are met:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Stab phlebectomy of varicose veins, 1-hyphen9 incisions, ambulatory - No specific code:</strong></td>
</tr>
<tr>
<td>36470</td>
<td>Injection of sclerosing solution; single vein</td>
</tr>
<tr>
<td>36471</td>
<td>multiple veins, same leg</td>
</tr>
<tr>
<td>36475</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated</td>
</tr>
<tr>
<td>+ 36476</td>
<td>second and subsequent veins treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>36478</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated</td>
</tr>
<tr>
<td>+ 36479</td>
<td>second and subsequent veins treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>37500</td>
<td>Vascular endoscopy, surgical, with ligation of perforator veins, subfascial (SEPS)</td>
</tr>
<tr>
<td>37700</td>
<td>Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions</td>
</tr>
<tr>
<td>Code</td>
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<tr>
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<tr>
<td>37718</td>
<td>Ligation, division, and stripping, short saphenous vein</td>
</tr>
<tr>
<td>37722</td>
<td>Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below</td>
</tr>
<tr>
<td>37735</td>
<td>Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia</td>
</tr>
<tr>
<td>37760</td>
<td>Ligation of perforator veins, subfascial, radical (Linton type), including skin graft, when performed, open, 1 leg</td>
</tr>
<tr>
<td>37761</td>
<td>Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg</td>
</tr>
<tr>
<td>37765</td>
<td>Stab phlebectomy of varicose veins, one extremity; 10-20 stab incisions [ambulatory]</td>
</tr>
<tr>
<td>37766</td>
<td>more than 20 incisions [ambulatory]</td>
</tr>
<tr>
<td>37780</td>
<td>Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)</td>
</tr>
<tr>
<td>37785</td>
<td>Ligation, division, and/or excision of varicose vein cluster(s), one leg</td>
</tr>
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</table>

**CPT codes not covered for indications listed in the CPB:**

<table>
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<th>Code</th>
<th>Code Description</th>
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</thead>
<tbody>
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<td>36011</td>
<td>Selective catheter placement, venous system; first order branch (e.g., renal vein, jugular vein)</td>
</tr>
<tr>
<td>36468</td>
<td>Single or multiple injections of sclerosing solutions, spider veins (telangiectasia); limb or trunk</td>
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<tr>
<td>Code</td>
<td>Code Description</td>
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<tr>
<td>37241</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicoceles)</td>
</tr>
<tr>
<td>37244</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for arterial or venous hemorrhage or lymphatic extravasation</td>
</tr>
<tr>
<td>75894</td>
<td>Transcatheter therapy, embolization, any method, radiological supervision and interpretation</td>
</tr>
<tr>
<td>76942</td>
<td>Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation [not covered when performed solely to guide the needle or introduce the sclerosant into the varicose veins]</td>
</tr>
<tr>
<td>76998</td>
<td>Ultrasonic guidance, intraoperative [not covered when performed solely to guide the needle or introduce the sclerosant into the varicose veins]</td>
</tr>
</tbody>
</table>

**Other CPT codes related to the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>37252</td>
<td>Intravascular ultrasound (noncoronary vessel) during diagnostic evaluation and/or therapeutic intervention, including radiological supervision and interpretation; initial noncoronary vessel (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>75820,</td>
<td>Venography, extremity, unilateral or bilateral, radiological supervision and interpretation</td>
</tr>
<tr>
<td>75822</td>
<td></td>
</tr>
<tr>
<td>93922</td>
<td>Limited bilateral non-invasive physiologic studies of upper or lower extremity arteries, (eg, for lower extremity: ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries plus bidirectional, Doppler waveform recording and analysis at 1-2 levels, or ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries plus volume plethysmography at 1-2 levels, or ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries with transcutaneous oxygen tension measurements at 1-2 levels)</td>
</tr>
<tr>
<td>93923</td>
<td>Complete bilateral non-invasive physiologic studies of upper or lower extremity arteries, 3 or more levels (eg, for lower extremity: ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries plus segmental blood pressure measurements with bidirectional Doppler waveform recording and analysis at 3 or more levels, or ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries plus segmental volume plethysmography at 3 or more levels, or ankle/brachial indices at distal posterior tibial and anterior tibial/dorsalis pedis arteries plus segmental transcutaneous oxygen tension measurements at 3 or more level(s), or single level study with provocative functional maneuvers (eg, measurements with postural provocative tests or measurements with reactive hyperemial)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>93924</td>
<td>Non-invasive physiologic studies of lower extremity arteries, at rest and following treadmill stress testing, (ie, bidirectional Doppler waveform or volume plethysmography recording and analysis at rest with ankle/brachial indices immediately after and at timed intervals following performance of a standardized protocol on a motorized treadmill plus recording of time of onset of claudication or other symptoms, maximal walking time, and time to recovery) complete bilateral study</td>
</tr>
<tr>
<td>93970</td>
<td>Duplex scan of extremity veins including responses to compression and other maneuvers; complete bilateral study</td>
</tr>
<tr>
<td>93971</td>
<td>unilateral or limited study</td>
</tr>
</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**

S2202  Echosclerotherapy

**Other HCPCS codes related to the CPB:**

A6530 - A6549  Compression stockings

**ICD-10 codes covered if selection criteria are met:**

I80.00 - I80.03  Phlebitis and thrombophlebitis of superficial vessels of lower extremities

I82.401 - I82.499  Acute embolism and thrombosis of deep veins of lower extremity

I82.501 - I82.599  Chronic embolism and thrombosis of deep veins of lower extremity

I83.001 - I83.899  Varicose veins of lower extremities

I87.001 - I87.09  Postthrombotic syndrome
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I87.2</td>
<td>Venous insufficiency (chronic) (peripheral) [not covered for saphenopopliteal reflux]</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I83.90 -</td>
<td>Asymptomatic varicose veins of lower extremities</td>
</tr>
<tr>
<td>I83.93</td>
<td></td>
</tr>
<tr>
<td>O22.00 -</td>
<td>Varicose veins of lower extremity in pregnancy</td>
</tr>
<tr>
<td>O22.03</td>
<td></td>
</tr>
<tr>
<td>O22.20 -</td>
<td>Superficial thrombophlebitis in pregnancy</td>
</tr>
<tr>
<td>O22.23</td>
<td></td>
</tr>
<tr>
<td>O22.90 -</td>
<td>Venous complication in pregnancy, unspecified</td>
</tr>
<tr>
<td>O22.93</td>
<td></td>
</tr>
<tr>
<td>O87.0</td>
<td>Superficial thrombophlebitis in the puerperium</td>
</tr>
<tr>
<td>O87.4</td>
<td>Varicose veins of lower extremity in the puerperium</td>
</tr>
<tr>
<td>O87.9</td>
<td>Venous complication in the puerperium, unspecified</td>
</tr>
</tbody>
</table>

**Mechanicochemical ablation (MOCA) (ClariVein):**

No specific code

**CPT codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36475</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated</td>
</tr>
<tr>
<td>+36476</td>
<td>second and subsequent veins treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>36478</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated</td>
</tr>
<tr>
<td>+36479</td>
<td>second and subsequent veins treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>

**CPT codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36473</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated</td>
</tr>
<tr>
<td>36474</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>37204</td>
<td>Transcatheter occlusion or embolization (eg, for tumor destruction, to achieve hemostasis, to occlude a vascular malformation), percutaneous, any method, non-central nervous system, non-head or neck</td>
</tr>
</tbody>
</table>

*Medical adhesive (cyanoacrylate superglue, n-butyl-cyanoacrylate) (e.g., VariClose Vein Sealing System, VenaSeal Closure System) - no specific code:

The above policy is based on the following references:
15. Jakobsen BH. The value of different forms of treatment for


39. Sadick NS. Commentary: Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of


50. Smith JJ, Brown L, Greenhalgh RM, Davies AH. Randomised


58. Allegra C. Abstract and Commentary: Efficacy of the comprehensive objective mapping, precise image-guided injection, anti-reflux positioning, and sequential sclerotherapy (COMPASS) Technique in the management of greater saphenous varicosities with saphenofemoral


95. National Institute for Clinical Excellence (NICE). Subfascial


among the diameter of the great saphenous vein, clinical state and haemodynamic pattern of the saphenofemoral junction in chronic superficial venous insufficiency. Phlebology. 2007;22(5):207-213.


156. Vun S, Rashid S, Blest N, Spark J. Lower pain and faster treatment with mechanico-chemical endovenous ablation


164. Todd KL 3rd, Wright DI; VANISH-2 Investigator Group. The VANISH-2 study: A randomized, blinded, multicenter study to evaluate the efficacy and safety of polidocanol endovenous microfoam 0.5% and 1.0% compared with placebo for the treatment of saphenofemoral junction incompetence. Phlebology. 2014;29(9):608-618.


193. Tang TY, Kam JW, Gaunt ME. ClariVein® - Early results from


202. Gibson K, Ferris B. Cyanoacrylate closure of incompetent


209. Nakano L. Mechanochemical ablation (MOCA) for superficial venous insufficiency. PROSPERO. 2017;CRD42017055127.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0050 Varicose Veins

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania

revised 3/9/2018