7.01.124	Treatment of Varicose Veins/Venous Insufficiency		
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Section:	7.0 Surgery	**Page:**	Page 1 of 44

Policy Statement

Great, Small, or Accessory Saphenous Veins

I. Saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met:
   A. Documentation to use **only one** of the following procedures (not combined use of different procedures or an unlisted procedure): surgery (ligation and stripping), radiofrequency endovenous thermal ablation, laser endovenous thermal ablation, microfoam sclerotherapy, or cyanoacrylate adhesion
   B. There is demonstrated saphenous reflux and CEAP (Clinical, Etiology, Anatomy, Pathophysiology) class C2 or greater
   C. There is documentation of **one or more** of the following:
      1. Ulceration secondary to venous stasis
      2. Recurrent superficial thrombophlebitis
      3. Hemorrhage or recurrent bleeding episodes from a ruptured superficial varicosity
      4. Persistent pain, swelling, itching, burning, or other symptoms are associated with saphenous reflux, and **both** of the following:
         a. The symptoms significantly interfere with activities of daily living
         b. Conservative management including compression therapy for at least 6 weeks has not improved the symptoms

II. Treatment of saphenous veins by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy or cyanoacrylate adhesive that does not meet the criteria described above is considered **investigational**.

III. Combining the use of **any two** medically necessary treatments (e.g., radiofrequency ablation [RFA] and microfoam sclerotherapy) during the same treatment session on the same vein or same type of vein is considered **not medically necessary**.

IV. Sclerotherapy techniques (other than microfoam sclerotherapy) as the primary treatment of great, small, or accessory saphenous veins, is considered **investigational.** However, standard foam sclerotherapy can be used for cleanup of small sections of saphenous veins when needed after primary treatment by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, or cyanoacrylate adhesive.

V. Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy of perforator, great, small, or accessory saphenous veins are considered **investigational.**

Symptomatic Varicose Tributaries

VI. Tributary varicosity treatment when performed either at the same time (or following prior treatment) as saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met:
   A. Documentation to use **one** of the following procedures (not an unlisted procedure): stab avulsion, hook phlebectomy, standard sclerotherapy (not including microfoam sclerotherapy), transilluminated powered phlebectomy
   B. Saphenous veins have been previously treated successfully or will be treated during the same session
   C. The tributaries are symptomatic

D. All tributaries in the same leg meeting criteria for treatment will be treated in the same session (or have documentation submitted when that should not be done)
E. Use of microfoam sclerotherapy or cyanoacrylate only when using leftover product during the same session as saphenous vein treatments using the same agent

VII. When done separately from saphenous vein treatment, the use of microfoam sclerotherapy (does NOT apply to standard foam sclerotherapy) or cyanoacrylate to treat symptomatic varicose tributaries is considered to be **investigational**, either:
A. On a different date as saphenous vein treatment
B. On the same date when saphenous vein treatment was done using a different modality (i.e., RFA, laser or surgery)

VIII. The following are considered **investigational**:
A. Treatment of isolated tributary veins without prior or concurrent treatment of saphenous veins
B. Isolated treatment of symptomatic varicose tributaries using any other techniques than those noted above
C. Endovenous radiofrequency or laser ablation of tributary veins

Perforator Veins

IX. Perforator vein treatments for leg ulcers may use surgical ligation (including Subfascial Endoscopic Perforator Surgery-SEPS) or endovenous thermal ablation (radiofrequency or laser), microfoam or standard foam sclerotherapy or cyanoacryolate adhesion may be considered **medically necessary** when **all** of the following conditions have been met:
A. There is demonstrated perforator reflux
B. Any superficial saphenous veins (great, small, or accessory saphenous and symptomatic varicose tributaries) have been previously eliminated
C. Ulcers are present that have not resolved following combined superficial vein treatment and compression therapy for at least 3 months
D. The venous insufficiency is not secondary to deep venous thromboembolism

X. Stab avulsion, hook phlebectomy, transilluminated powered phlebectomy of perforator veins are considered **investigational.**

Telangiectasia

XI. Treatment of telangiectasia such as spider veins, angiomata, and hemangiomata that are less than 3 millimeters in diameter are considered **investigational**.

Miscellaneous

XII. The following are considered **investigational**:
A. Mechanochemical ablation (MOCA) of any vein
B. Endovenous cryoablation of any vein

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Documentation for Tributary Vein Treatments

If veins in a leg meeting criteria for treatment are planned to be treated during different sessions, documentation should include:

- For microfoam or cyanoacrylate, why manufacturer's literature on maximum dose per session would be exceeded

- For procedures requiring tumescent anesthesia, why a lower concentration of lidocaine (such as 0.05%) cannot be used
- For treatment of multiple tributaries, why individual position cannot be changed as needed to complete all necessary procedures

Microfoam Sclerotherapy

Described in the CPT code as "non-compounded foam sclerosant," the term microfoam refers to the brand name Varithena®, which uses a special blend of gases to create uniform, small bubbles. This is different from standard foam sclerotherapy which comes as a liquid (and can be the same basic agent as Varithena®) that can be used directly (as a liquid) or mixed back and forth using syringes to make it foamy. But the resulting standard foam does not have the same uniformly small bubbles as microfoam, so it performs differently in larger veins.

Tributary Treatment Sessions

Tributary treatments do not need to be done at the same time as saphenous vein treatments. However, all tributary varicose veins that are documented as being medically necessary to treat should be treated during the same session unless documented as medically contraindicated (e.g., pain, anesthesia risk, etc.). If more than one session is needed for medical reasons, treatment should be done in the fewest sessions possible. Separate requests will need to be made for additional treatments (after completion of initial treatment, including results).

Multiple tributaries can be treated in the same session and is the preferred method (CPT code 36471). Separate sessions each treating a single vein (CPT code 36470) is not needed. The need for multiple sessions treating multiple tributaries needs to be clearly documented for more than one session to be approved during the same request.

Classification of Venous Disease

The standard classification of venous disease is the CEAP (Clinical, Etiologic, Anatomic, Pathophysiologic) classification system. Table PG1 provides the Clinical portion of the CEAP.

Table PG1. Clinical Portion of the CEAP Classification System

Class	Definition
C_0	No visible or palpable signs of venous disease
C_1	Telangiectasies or reticular veins
C_2	Varicose veins
C_{2r}	Recurrent varicose veins
C_3	Edema
C_4	Changes in skin and subcutaneous tissue secondary to CVD
C_{4a}	Pigmentation and eczema
C_{4b}	Lipodermatosclerosis or atrophie blanche
C_{4C}	Corona phlebectatica
C_5	Healed
C_6	Active venous ulcer
C_{6r}	Recurrent active venous ulcer
S	Symptomatic
A	Asymptomatic

Adapted from: https://www.jvsvenous.org/article/S2213-333X(20)30063-9/pdf
CEAP: Clinical, Etiologic, Anatomic, Pathophysiologic classification system; CVD, chronic venous disease. Each clinical class subcharacterized by a subscript indicates the presence (symptomatic, s) or absence (asymptomatic, a) of symptoms attributable to venous disease.

Coding

All of the following are incidental to the primary procedure and not separately reimbursable:

- All imaging guidance and monitoring (Doppler or Duplex ultrasound, or fluoroscopy) performed during the procedure (surgery, sclerotherapy, ablation, etc.) or for the purpose of mapping
- Endovenous balloon isolation (balloon sclerotherapy) using a double lumen balloon catheter for sclerotherapy
- Injection procedures with or without automatic power injection
- Introduction of needles or catheters
- Local anesthesia
- Sedation
- Use of optical magnifying glasses (loupes)
- Vascular access including venipuncture
- Microfoam, standard foam or liquid sclerosants, and cyanoacrylate are included in the fees paid for the procedures and are not paid separately or in addition to procedure fees

Coding
See the Codes table for details.

Description

A variety of treatment modalities are available to treat varicose veins/venous insufficiency, including surgery, thermal ablation, sclerotherapy, mechanochemical ablation (MOCA), cyanoacrylate adhesive (CAC), and cryotherapy. The application of each modality is influenced by the severity of the symptoms, type of vein, source of venous reflux, and the use of other (prior or concurrent) treatment.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In 2015, the VenaSeal™ Closure System (Sapheon, part of Medtronic) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (P140018) process for the permanent closure of clinically significant venous reflux through endovascular embolization with coaptation. The VenaSeal Closure System seals the vein using a cyanoacrylate adhesive agent. FDA product code: PJQ.

In 2013, Varithena® (formerly Varisolve), a sclerosant microfoam made with a proprietary gas mix, was approved by the FDA under a new drug application (205-098) for the treatment of incompetent

great saphenous veins, accessory saphenous veins, and visible varicosities of the great saphenous vein system above and below the knee.

The following devices were cleared for marketing by the FDA through the 510(k) process for endovenous treatment of superficial vein reflux:

In 1999, the VNUS Closure® System, a radiofrequency device, was cleared by the FDA through the 510(k) process for "endovascular coagulation of blood vessels in patients with superficial vein reflux." In 2005, the VNUS RFS® and RFS*Flex®* devices were cleared by the FDA for "use in vessel and tissue coagulation including treatment of incompetent (i.e., refluxing) perforator and tributary veins." In 2008, the modified VNUS ClosureFast® Intravascular Catheter was cleared by the FDA through the 510(k) process. FDA product code: GEI.

In 2002, the Diomed 810 nm surgical laser and EVLT® (endovenous laser therapy) procedure kit were cleared by the FDA through the 510(k) process ".....for use in the endovascular coagulation of the great saphenous vein of the thigh in patients with superficial vein reflux." FDA product code: GEX. In 2005, a modified Erbe Erbokryo cryosurgical unit (Erbe USA) was approved by the FDA for marketing through the 510(k) process. A variety of clinical indications are listed, including cryostripping of varicose veins of the lower limbs. FDA product code: GEH.

In 2003, the Trivex system (InaVein), a device for transilluminated powered phlebectomy, was cleared by the FDA through the 510(k) process for "ambulatory phlebectomy procedures for the resection and ablation of varicose veins." FDA product code: DNQ.

In 2008, the ClariVein® Infusion Catheter (Merit Medical) was cleared by the FDA through the 510(k) process (K071468) for mechanochemical ablation. The FDA determined that this device was substantially equivalent to the Trellis Infusion System (K013635) and the Slip-Cath Infusion Catheter (K882796). The system includes an infusion catheter, motor drive, stopcock, and syringe, and is intended for the infusion of physician-specified agents in the peripheral vasculature. FDA product code: KRA

Rationale

Background

Venous Reflux/Venous Insufficiency

The venous system of the lower extremities consists of the superficial veins (this includes the great and small saphenous and accessory, or duplicate, veins that travel in parallel with the great and small saphenous veins), the deep system (popliteal and femoral veins), and perforator veins that cross through the fascia and connect the deep and superficial systems. One-way valves are present within all veins to direct the return of blood up the lower limb. Because the venous pressure in the deep system is generally greater than that of the superficial system, valve incompetence at any level may lead to backflow (venous reflux) with pooling of blood in superficial veins. Varicose veins with visible varicosities may be the only sign of venous reflux, although itching, heaviness, tension, and pain may also occur. Chronic venous insufficiency secondary to venous reflux can lead to thrombophlebitis, leg ulcerations, and hemorrhage. The CEAP classification of venous disease considers the clinical, etiologic, anatomic, and pathologic characteristics of venous insufficiency, ranging from class 0 (no visible sign of disease) to class 6 (active ulceration).

Treatment of Saphenous Veins and Tributaries

Saphenous veins include the great and small saphenous and accessory saphenous veins that travel in parallel with the great or small saphenous veins. Tributaries are veins that empty into a larger vein. Treatment of venous reflux has traditionally included the following:

- Identification by preoperative Doppler ultrasonography of the valvular incompetence.

- Control of the most proximal point of reflux, traditionally by suture ligation of the incompetent saphenofemoral or saphenopopliteal junction.
- Removal of the superficial vein from circulation, e.g., by stripping of the great and/or small saphenous veins.
- Removal of varicose tributaries (at the time of the initial treatment or subsequently) by stab avulsion (phlebectomy) or injection sclerotherapy.

Minimally invasive alternatives to ligation and stripping have been investigated. These include forms of sclerotherapy, cyanocrylate adhesive, and thermal ablation using cryotherapy, high-frequency radio waves (200 to 300 kHz), or laser energy.

Thermal Ablation

Radiofrequency ablation (RFA) is performed using a specially designed catheter inserted through a small incision in the distal medial thigh to within 1 to 2 cm of the saphenofemoral junction. The catheter is slowly withdrawn, closing the vein. Laser ablation is performed similarly. A laser fiber is introduced into the great saphenous vein under ultrasound guidance. The laser is then activated and slowly removed, along the course of the saphenous vein. Cryoablation uses extreme cold. The objective of endovenous techniques is to injure the vessel, causing retraction and subsequent fibrotic occlusion of the vein. Technical developments since thermal ablation procedures were initially introduced include the use of perivenous tumescent anesthesia, which allows successful treatment of veins larger than 12 mm in diameter and helps to protect adjacent tissue from thermal damage during treatment of the small saphenous vein.

Sclerotherapy

The objective of sclerotherapy is to destroy the endothelium of the target vessel by injecting an irritant solution (either a detergent, osmotic solution, or chemical irritant), ultimately occluding the vessel. Treatment success depends on accurate injection of the vessel, an adequate injectate volume and concentration of sclerosant, and compression. Historically, larger veins and very tortuous veins were not considered good candidates for sclerotherapy due to technical limitations. Technical improvements in sclerotherapy have included the routine use of Duplex ultrasound to target refluxing vessels, luminal compression of the vein with anesthetics, and a foam/sclerosant injectate in place of liquid sclerosant. Foam sclerosants are produced by forcibly mixing a gas (e.g., air or carbon dioxide) with a liquid sclerosant (e.g., polidocanol or sodium tetradecyl sulfate). Physician-compounded foam is produced at the time of treatment. A commercially available microfoam sclerosant with a proprietary gas mix is available and is proposed to provide a smaller and more consistent bubble size than what is produced with physician-compounded sclerosant foam.

Endovenous Mechanochemical Ablation

Endovenous mechanochemical ablation uses both sclerotherapy and mechanical damage to the lumen. Following ultrasound imaging, a disposable catheter with a motor drive is inserted into the distal end of the target vein and advanced to the saphenofemoral junction. As the catheter is pulled back, a wire rotates at 3500 rpm within the lumen of the vein, abrading the lumen. At the same time, a liquid sclerosant (sodium tetradecyl sulfate) is infused near the rotating wire. It is proposed that mechanical ablation allows for better efficacy of the sclerosant, and results in less pain and risk of nerve injury without the need for the tumescent anesthesia used with endovenous thermal ablation techniques (RFA, endovenous laser ablation).

Cyanoacrylate Adhesive

A cyanoacrylate adhesive is a clear, free-flowing liquid that polymerizes in the vessel via an anionic mechanism (i.e., polymerizes into a solid material on contact with body fluids or tissue). The adhesive is gradually injected along the length of the vein in conjunction with ultrasound and manual compression. The acute coaptation halts blood flow through the vein until the implanted adhesive becomes fibrotically encapsulated and establishes chronic occlusion of the treated vein. Cyanoacrylate glue has been used as a surgical adhesive and sealant for a variety of indications,

including gastrointestinal bleeding, embolization of brain arteriovenous malformations, and surgical incisions or other skin wounds.

Transilluminated Powered Phlebectomy

Transilluminated powered phlebectomy is an alternative to stab avulsion and hook phlebectomy. This procedure uses 2 instruments: an illuminator, which also provides irrigation, and a resector, which has an oscillating tip and suction pump. Following removal of the saphenous vein, the illuminator is introduced via a small incision in the skin and tumescence solution (anesthetic and epinephrine) is infiltrated along the course of varicosity. The resector is then inserted under the skin from the opposite direction, and the oscillating tip is placed directly beneath the illuminated veins to fragment and loosen the veins from the supporting tissue. Irrigation from the illuminator is used to clear the vein fragments and blood through aspiration and additional drainage holes. The illuminator and resector tips may then be repositioned, thereby reducing the number of incisions needed when compared with stab avulsion or hook phlebectomy. It has been proposed that transilluminated powered phlebectomy might decrease surgical time, decrease complications such as bruising, and lead to a faster recovery than established procedures.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.
To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Treatment of Saphenous Veins

Clinical Context and Therapy Purpose

Treatment of venous reflux/venous insufficiency seeks to reduce abnormal pressure transmission from the deep to the superficial veins. Conservative medical treatment consists of elevation of the extremities, graded compression, and wound care when indicated. Conventional surgical treatment consists of identifying and correcting the site of reflux by ligation of the incompetent junction followed by stripping of the vein to redirect venous flow through veins with intact valves. While most venous reflux is secondary to incompetent valves at the saphenofemoral or saphenopopliteal junctions, reflux may also occur at incompetent valves in the perforator veins or the deep venous system. The competence of any single valve is not static and may be pressure-dependent. For

example, accessory saphenous veins may have independent saphenofemoral or saphenopopliteal junctions that become incompetent when the great or small saphenous veins are eliminated, and blood flow is diverted through the accessory veins.

The following section addresses the efficacy of the conventional treatments, specifically on the appropriate length of a trial of compression therapy and evaluation of recurrence rates for surgical treatment (i.e., ligation and stripping) compared with compression therapy.

Compression Therapy

A Cochrane review by O'Meara et al (2009) evaluating compression for venous leg ulcers included 39 RCTs with 47 different comparisons.[1,] This review was updated in 2012 and included 48 RCTs with 59 different comparisons.[2,] Most RCTs were small. Measures of healing were the time to complete healing, the proportion of ulcers healed within the trial period (typically 12 weeks), the change in ulcer size, and the rate of change in ulcer size. Evidence from 8 trials indicated that venous ulcers healed more rapidly with compression than without. Findings suggested that multicomponent systems (bandages or stockings) were more effective than single-component compression. Also, multicomponent systems containing an elastic bandage appeared more effective than those composed mainly of inelastic constituents. Although these meta-analyses did not include time to healing, studies included in the review reported that the mean time to ulcer healing was approximately 2 months, while the median time to healing in other reports was 3 to 5 months.
A Cochrane review by Knight Nee Shingler et al (2021) assessed compression stockings as an initial treatment for varicose veins in patients without venous ulceration.[3,] This is the second update of a review first published in 2011. Thirteen studies involving 1021 participants with varicose veins without healed or active venous ulceration (CEAP [Clinical, Etiology, Anatomy, Pathophysiology] class C2 to C4) were selected. Compression ranged from 10 to 50 mmHg among studies. Studies could not be pooled for analysis due to heterogeneity in outcomes and method of assessment leading to a low or very low certainty of evidence. Using compression stockings compared to no treatment or placebo stockings led to subjective improvement in symptoms but this finding could be biased because the change in symptoms was not compared to the control arm in all studies. Studies that compared different compression stockings also found subjective improvement in symptoms from baseline to the end of the study, but the change in symptoms was not always compared between groups. The authors were unable to make conclusions about the optimal stocking pressure or length of stocking exposure from the included studies. Reviewers concluded that there was insufficient high-quality evidence to determine whether compression stockings were effective as the sole and initial treatment of varicose veins in patients without venous ulceration, or whether any type of stocking was superior to another type.

Ligation and Stripping

Systematic literature reviews have indicated a similar healing rate of venous ulcers with superficial vein surgery and conservative compression treatments but a reduction in ulcer recurrence rate with surgery.[4,5,] In general, recurrence rates after ligation and stripping are estimated at 20% in short-term follow-up. Jones et al (1996) reported on the results of a trial that randomized 100 patients with varicose veins to ligation alone or ligation plus stripping.[6,] At 1 year, reflux was detected in 9% of patients, rising to 26% at 2 years. Rutgers and Kitslaar (1994) reported on the results of a trial that randomized 181 limbs to ligation and stripping or to ligation plus sclerotherapy.[7,] At 2 years, Doppler ultrasound demonstrated reflux in approximately 10% of patients after ligation and stripping, increasing to 15% at 3 years.

Alternatives to Ligation and Stripping

The purpose of endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, mechanochemical ablation (MOCA), cyanoacrylate adhesive (CAC), or cryoablation in individuals who have varicose veins/venous insufficiency and saphenous vein reflux is to provide a treatment option that is an alternative to or an improvement on existing treatments.

The following PICO was used to select literature to inform this review.

Populations
The relevant populations of interest are those who have varicose veins/venous insufficiency and saphenous vein reflux.

Interventions
The therapies being considered are endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, MOCA, CAC, or cryoablation.

Comparators
Established treatments for varicose veins/venous insufficiency and saphenofemoral junction reflux are conservative therapy with compression bandages and ligation and stripping, with which the endovenous thermal procedures are compared. The less invasive endovenous thermal ablation (radiofrequency or laser) have become the standard treatments by which the newer treatments are compared. Endovenous thermal ablation techniques require tumescent anesthesia, which involves multiple injections along the vein and is associated with moderate pain. Compression stockings and avoidance of strenuous activities are recommended. Procedures that have more recently been developed (MOCA, CAC, and cryotherapy) do not require tumescent anesthesia and are compared with thermal ablation procedures.

Outcomes
Outcomes of interest for venous interventions include healing and recurrence, recanalization of the vein, and neovascularization. Recanalization is the restoration of the lumen of a vein after it has been occluded; this occurs more frequently following treatment with endovenous techniques. Neovascularization is the proliferation of new blood vessels in tissue and occurs more frequently following vein stripping. Direct comparisons of the durability of endovenous and surgical procedures are complicated by these mechanisms of recurrence. Relevant safety outcomes include the incidence of paresthesia, thermal skin injury, thrombus formation, thrombophlebitis, wound infection, and transient neurologic effects.

Specific measures may include the visual analog score (VAS) for pain, the Venous Clinical Severity Score (VCSS), and the Aberdeen Varicose Veins Questionnaire (AVVQ). AVVQ scores range from 0 to 100 (worst possible quality of life). Follow-up at 1 and 2 years from RCTs is of interest to monitor treatment success (vein occlusion and recanalization), with follow-up to 5 years to assess the durability of treatment.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Treatment of Saphenous Veins: Endovenous Thermal Ablation (Laser or Radiofrequency)

Systematic Reviews
Farah et al (2022) conducted a systematic review and meta-analysis that informed the 2022 mutiorganization guideline on management of varicose veins.[8,] The review addressed 3 key questions related to treatment: whether there is a benefit of surgical stripping versus endovenous ablation,

whether there is a benefit of thermal versus nonthermal ablation techniques, and whether ablation of incompetent perforator veins improves outcomes. Multiple outcomes of interest were assessed at various time points for each question. For the first key question, an analysis of 30 RCTs and 16 observational studies found few studies that reported the outcomes of interest at each time point (between 1 month and 5 years), but anatomic closure was better with surgical stripping compared to endovenous ablation techniques. Analysis for the second question included 16 RCTs and 11 observational studies, few of which included the outcomes of interest at the time points of interest. Overall, endovenous laser ablation resulted in higher rates of anatomical closure at 1 year and 5 years versus nonthermal ablation techniques.

A Cochrane review by Whing et al (2021) compared interventions for great saphenous vein incompetence.[9,] The review included 24 RCTs (N=5135) and the duration of follow-up for included trials ranged from 5 weeks to 8 years. When comparing endovenous laser ablation to ligation and stripping, pooled data from 6 RCTs (n=1051) suggest that technical success may be better with endovenous laser ablation up to 5 years (odds ratio [OR], 2.31, 95% confidence interval [CI], 1.27 to 4.23; low-certainty evidence), but not at 5 years and beyond based on data from 5 RCTs (n=874). The risk of recurrence is similar between treatments within 3 years and at 5 years based on data from 7 RCTs each (n=1459 and n=1267, respectively). When comparing radiofrequency ablation (RFA) to ligation and stripping, data from 2 RCTs (n=318) suggest that there is no significant difference in the rate of technical success up to 5 years; data from 1 RCT (n=289) with duration over 5 years also suggest no significant difference between treatments. Based on data from 4 RCTs (n=546), there is no significant difference in the risk of recurrence up to 3 years; but based on 1 trial (n=289), a possible long-term benefit for RFA is observed (OR, 0.41, 95% CI, 0.22 to 0.75; low-certainty evidence). When comparing endovenous laser ablation with RFA, technical success is comparable up to 5 years and over 5 years. Based on data from 1 study (n=291), there is no significant difference in the risk of recurrence between treatments at 3 years, but a benefit for RFA over endovenous laser ablation may be seen at 5 years (OR, 2.77 ; 95% CI, 1.52 to 5.06).

A Cochrane review by Paravastu et al (2016) compared endovenous laser ablation or RFA with surgical repair for small saphenous veins with reflux at the saphenopopliteal junction.[10,] Three RCTs identified compared endovenous laser ablation with surgery. There was moderate-quality evidence that recanalization or persistence of reflux at 6 weeks occurred less frequently after endovenous laser ablation than after surgery (OR, 0.07 ; 95% CI, 0.02 to 0.22), and low-quality evidence that recurrence of reflux was lower after endovenous laser ablation at 1 year (OR, 0.24 ; 95% CI, 0.07 to 0.77).

Randomized Controlled Trials

The largest RCT was reported by Brittenden et al (2014) and compared foam sclerotherapy, endovenous laser ablation, and surgical treatment in 798 patients.[11,] The trial was funded by the U.K.'s National Institute for Health Research. Veins greater than 15 mm in diameter were excluded from the trial. At the 6-week follow-up visit, patients assigned to treatment with foam or laser had the option of treatment with foam for any residual varicosities. This optional treatment was performed in 38% of patients in the foam group and 31% of patients in the endovenous laser ablation group. Disease-specific quality of life was similar for the laser and surgery groups. The frequency of procedural complications was similar for the foam sclerotherapy (6%) and surgery (7%) groups but was lower for the laser group (1%).

The 2012 Randomized Study Comparing Endovenous Laser Ablation with Crossectomy and Stripping of the Great Saphenous Vein (RELACS) study randomized 400 patients to endovenous laser ablation performed by a surgeon at 1 site or to ligation and stripping performed by a different surgeon at a second location.[12,] At 2-year follow-up, there were no significant differences between groups for clinically recurrent varicose veins, medical condition measured on the Homburg Varicose Vein Severity Score, or disease-related quality of life. Saphenofemoral reflux was detected by ultrasonography more frequently after endovenous laser treatment (17.8% vs. 1.3%). The follow-up rate at 5 years was 81%.[13,] Same-site recurrences were more frequent in the endovenous laser

ablation group (18% with endovenous laser ablation vs. 5% with surgery ; p=.002), but different-site recurrences were more frequent in the surgically treated group (50% with surgery vs. 31% with endovenous laser ablation ; p=.002). Overall, there was no significant difference in recurrence rates between groups. There were also no significant differences between groups in disease severity or quality of life at 5 years.

Christenson et al (2010) compared endovenous laser ablation with ligation and stripping in 200 limbs (100 in each group).[14,] At 1-year follow-up, 98% of the limbs were reported to be free of symptoms. At 2-year follow-up, the endovenous laser ablation group had 2 veins completely reopened and 5 partially reopened, which was significantly greater than in the ligation and stripping group. In the 2013 Comparative Study of the Treatment of Insufficient Greater Saphenous Vein: Surgery vs Ultrasound Guided Sclerotherapy With Foam and Endovenous Laser Therapy (MAGNA) trial, 223 consecutive patients (240 legs) with great saphenous vein reflux were randomized to endovenous laser ablation, ligation and stripping, or foam sclerotherapy.[15,] At 1-year follow-up, the anatomic success rates were similar for endovenous laser ablation (88.5%) and stripping (88.2%), which were both superior to foam sclerotherapy (72.2%). Ten percent of the stripping group showed neovascularization. At 5 years, health-related quality of life and CEAP classification improved in all groups with no significant differences among them.[16,] Grade I neovascularization was higher in the conventional surgery group (27% vs. 3% ; p<.001), while grade II neovascularization did not differ significantly between surgical (17%) and endovenous laser ablation (13%) groups.

Wallace et al (2018) published the 5-year outcomes of an RCT consisting of endovenous laser ablation compared with conventional surgery as treatments for symptomatic great saphenous varicose veins.[17,] Data from 218 patients were available at the 5-year follow-up. The clinical recurrence rate was 34.4% for the surgery group and 20.9% for endovenous laser ablation (p=.010). Patients' quality of life, assessed using EuroQol Five Dimensions (EQ-5D) and AVVQ, was significantly improved from baseline for both surgery (EQ-5D: 0.859 to 1.0, p=.002; AVVQ: 13.69 to 4.59, p<.001) and endovenous laser ablation (EQ-5D: 0.808 to 1.0, p=.002; AVVQ: 12.73 to 3.35, p<.001). Technical success assessed by duplex ultrasound examination was 85.4% for surgery and 93.2% for endovenous laser ablation (p=.074).

Tables 1 and 2 provide a summary of key characteristics and results, respectively, of these RCTs. The primary limitation of all studies was a lack of blinding.

Table 1. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Brittenden et al (2014)[11,]	UK	11	2008-2012	Individuals with primary varicose veins	Foam sclero-therapy (n=286) or endovenous laser ablation (n=210)	Surgical treatment (n=289)
Rass et al (2012);[12,] RELACS	US	2	2004-2007	Individuals with great saphenous vein insufficiency	Endovenous laser ablation (n=185)	Surgical treatment (n=161)
Wallace et al (2018)[17,]	UK	1	2004-2009[1]	Individuals with great saphenous vein insufficiency	Endovenous laser ablation (n=108)	Surgical treatment (n=110)

RCT: randomized controlled trial.
[1] Date of original intervention study

Table 2. Summary of Key RCT Results

Study	AVVQ Score at Baseline; 6 Months	Frequency of Procedural Complications	Rate of Same-Site Recurrence	Clinically Recurrent Varicose Veins	AVVQ Score at Baseline; 5 years
Brittenden et al (2014)[11,]					
Foam	17.69.9; 9.17.9	6%			
Laser	17.89.1; 7.98.4	1%			
Surgery	18.29.1; 7.87.5	7%			
p-value		<.001			
Rass et al (2012);[12,] RELACS					
Laser			18%	16.2%	
Surgery			5%	23.1%	
p-value			.002	.15	
Wallace et al (2018)[17,]					
Laser				20.9%	13.69; 4.59
Surgery				34.3%	12.73; 3.35
p-value				.010	<.001

AVVQ: Aberdeen Varicose Veins Questionnaire; RELACS: Randomized Study Comparing Endovenous Laser Ablation with Crossectomy and Stripping of the Great Saphenous Vein; RCT: randomized controlled trial.

The literature on the isolated treatment of the anterior accessory saphenous vein is relatively limited. A systematic review by Alozai et al (2021) identified 16 studies that evaluated treatment modalities for anterior accessory saphenous vein incompetence.[18,] All included studies were of moderate to poor quality. The pooled anatomic success rates were 91.8% after endovenous laser ablation and RFA (n=11 studies), 93.6% after CAC (n=3 studies), and 79.8% after sclerotherapy (n=2 studies).

Subsection Summary: Endovenous Thermal Ablation (Laser or Radiofrequency)

There are multiple large RCTs and systematic reviews of RCTs assessing endovenous ablation using radiofrequency or laser energy of the saphenous veins. Comparison with ligation and stripping at 2- to 5-year follow-up has indicated similar recurrence rates for the different treatments. Evidence has suggested that ligation and stripping may lead to neovascularization, while thermal ablation may lead to recanalization, resulting in similar outcomes for endovenous thermal ablation and surgery. Laser ablation and RFA have similar success rates.

Treatment of Saphenous Veins: Sclerotherapy

Systematic Reviews

A Cochrane review by Whing et al (2021) that compared interventions for great saphenous vein incompetence was introduced above.[9,] Based on pooled data from 4 RCTs (n=954), ultrasound-guided foam sclerotherapy was inferior to ligation and stripping for technical success up to 5 years (OR, 0.32 ; 95% CI, 0.11 to 0.94; low-certainty evidence), and beyond 5 years based on 3 RCTs (n=525)(OR, 0.09 ; 95% CI, 0.03 to 0.30; moderate-certainty evidence). There was no significant difference between treatments for recurrence up to 3 years based on 3 RCTs (n=822) and beyond 5 years based on 3 RCTs (n=639). Similarly, technical success was improved with endovenous laser ablation over ultrasound-guided foam sclerotherapy up to 5 years based on data from 3 RCTs (n=588) (OR, 6.13 ; 95% CI, 0.98 to 38.27; low-certainty evidence), and beyond 5 years based on data from 3 RCTs (n=534) (OR, 6.47 ; 95% CI, 2.60 to 16.10; low-certainty evidence). There was no significant difference between endovenous laser ablation and ultrasound-guided foam sclerotherapy for recurrence up to 3 years based on data from 2 RCTs (n=443), and at 5 years based on data from 2 RCTs (n=418).

Hamann et al (2017) conducted a meta-analysis of RCTs reporting 5-year follow-up.[19,] The meta-analysis (3 RCTs, 10 follow-up studies) included 611 legs treated with endovenous laser ablation, 549 treated with high ligation and stripping, 121 with sclerotherapy, and 114 with high ligation and

endovenous laser ablation. Ultrasound-guided sclerotherapy had significantly worse outcomes than the other 3 treatments, with anatomic success rates of 34% for sclerotherapy compared with 83% to 88% for the other 3 treatments (p<.001).

Physician-Compounded Sclerotherapy

Randomized Controlled Trials

In the 2013 MAGNA trial (previously described), 223 consecutive patients (240 legs) with great saphenous vein reflux were randomized to endovenous laser ablation, ligation and stripping, or physician-compounded foam sclerotherapy (1 mL aethoxysclerol 3%: 3 cc air).[15,] At 1-year follow-up, the anatomic success rate of foam sclerotherapy (72.2%) was inferior to both endovenous laser ablation (88.5%) and stripping (88.2%). Twenty-one patients in the sclerotherapy group had partial occlusion with reflux, though the clinical complaint was completely relieved. At 5-year follow-up, obliteration or absence of the great saphenous vein was observed in only 23% of patients treated with sclerotherapy compared with 85% of patients who underwent conventional surgery and 77% of patients who underwent endovenous laser ablation.[16,] Thirty-two percent of legs treated initially with sclerotherapy required 1 or more reinterventions during follow-up compared with 10% in the conventional surgery and endovenous laser ablation groups. However, clinically relevant grade II neovascularization was higher in the conventional surgery (17%) and endovenous laser ablation (13%) groups than in the sclerotherapy group (4%). EQ-5D scores improved equally in all groups.

Vahaaho et al (2018) published a study looking at the 5-year follow-up of patients with symptomatic great saphenous vein insufficiency.[20,] Between 2008 and 2010, 166 individuals were randomized to receive open surgery, endovenous laser ablation, or ultrasound-guided foam sclerotherapy. The great saphenous vein occlusion rate was 96% (95% CI, 91% to 100%) for open surgery, 89% (95% CI, 82% to 98%) for endovenous laser ablation, and 51% (95% CI, 38% to 64%) for ultrasound-guided foam sclerotherapy (p<.001). For patients with no additional treatment during follow-up, occlusion rates for open surgery, endovenous laser ablation, and ultrasound-guided foam sclerotherapy were 96%, 89%, and 41%, respectively. The study was limited by a lack of blinding and by non-standardized foam application.

Hamel-Desnos et al (2023) conducted a randomized trial of endovenous laser ablation versus physician-compounded foam sclerotherapy (0.5 mL polidocanol at concentrations ranging from 1% to 3% depending on vessel diameter; 2 mL air) in 161 patients with isolated small saphenous vein incompetence.[21,] Tributary vein treatments were not allowed for the first 6 months after the procedure. After the first 6 months, 33% of patients who received sclerotherapy and 19% of patients who received endovenous laser ablation received tributary treatment. The primary endpoint, absence of reflux in the treated segment at 3 years, was achieved in 86% of patients who received endovenous laser ablation versus 56% of patients who received sclerotherapy (risk ratio, 1.59; 95% CI, 1.26 to 2.01). Rates of partial and total failure were higher in the sclerotherapy group than the endovenous laser ablation group. Limitations include the pragmatic design that allowed clinicians to treat patients according to their normal practice except for the study intervention and a lack of blinding.

Non-randomized Comparative Studies

A noninferiority trial by Shadid et al (2012) compared foam sclerotherapy with ligation and stripping in 430 patients.[22,]The analysis was per protocol. Forty (17%) patients had repeat sclerotherapy. At 2 years, the probability of clinical recurrence was similar in both groups (11.3% sclerotherapy vs. 9.0% ligation and stripping), although reflux was significantly more frequent in the sclerotherapy group (35% vs. 21%). Thrombophlebitis occurred in 7.4% of patients after sclerotherapy. Two serious adverse events in the sclerotherapy group (deep venous thrombosis, pulmonary emboli) occurred within 1 week of treatment. Lam et al (2018) reported 8-year follow-up with 53% of the patients in the original trial.[23,] All measures of treatment success (e.g., symptomatic great saphenous vein reflux, saphenofemoral junction failure, and recurrent reflux in the great saphenous vein) were lower in the physician-compounded sclerotherapy group compared to the ligation and stripping group.

Microfoam Sclerotherapy

Randomized Controlled Trials

In 2013, polidocanol microfoam (Varithena) was approved under a new drug application for the treatment of varicose veins. Efficacy data were derived from 2 randomized, blinded, multicenter studies.[24,] One compared polidocanol at 0.5%, 1.0%, and 2.0% with endovenous placebo or a subtherapeutic dose of polidocanol foam. The primary endpoint was an improvement in symptoms at week 8, as measured by the Varicose Vein Symptoms Questionnaire. The improvement in symptoms was greater in the pooled polidocanol treatment group (p<.001) and in each of the individual dose-concentration groups compared with vehicle alone. Secondary and tertiary endpoints (appearance, duplex ultrasound response, quality of life) were also significantly better for the polidocanol groups compared with controls. The second study, VANISH-2, was published by Todd et al (2014).[25,] At the 8-week assessment, there was elimination of reflux and/or occlusion of the previously incompetent vein in 85.6% of the combined 0.5% and 1.0% groups, 59.6% of patients in the 0.125% group, and 1.8% of the placebo group. Analysis of data from both studies showed a dose-response from 0.5% to 2.0% for improvement in appearance and from 0.5% to 1.0% for Duplex responders. The polidocanol 1.0% dose was selected for the U.S. Food and Drug Administration (FDA) approval. Safety analysis found deep vein thrombosis detected by ultrasound in 2.8% of polidocanol-treated patients, with 1% of patients having proximal symptomatic thrombi; these patients were treated with anticoagulants. There was no sign of an increase in neurologic adverse events, and there were no adverse cardiac or cardiopulmonary effects following treatment with polidocanol injectable foam. Rates of occlusion with Varithena are similar to those reported for endovenous laser ablation or stripping. A randomized trial comparing endovenous laser ablation and stripping with this new preparation of foam sclerotherapy is needed to evaluate its comparative effectiveness. Evaluation out to 5 years is continuing.

Vasquez et al (2017) reported on a double-blind RCT that evaluated the addition of polidocanol microfoam to endovenous thermal ablation.[26,] A total of 117 patients who were candidates for both endovenous thermal ablation and treatment of visible varicosities received endovenous thermal ablation plus placebo (n=38) or polidocanol 0.5% (n=39) or 1% (n=40). At 8-week follow-up, physician-blinded vein appearance was significantly better with the combined polidocanol groups (p=.001), but the improvement in patient ratings was not statistically significant. At 6-month follow-up, the percentages of patients who achieved a clinically meaningful change were significantly higher in both physician (70.9% vs. 42.1% ; p=.001) and patient (67% vs. 50% ; p=.034) ratings. The proportion of patients who received additional treatment for residual varicosities between week 8 and month 6 was modestly reduced (13.9% for the polidocanol vs. 23.7% for placebo ; p=.037).

Retrospective Studies

Deak (2018) reported results from a retrospective review of 250 patients with symptomatic chronic venous insufficiency who were treated with polidocanol microfoam in a community practice.[27,] Patients who had tortuous veins that were not accessible with a catheter or who had a history of a previous vein ablation procedure with scarring in the lumen were selected for treatment with the microfoam scleroscant. It was reported that some patients required additional treatments between 5 days and 2 years for the vein to close, but the publication did not report how many additional treatments were given. After all the treatments were completed, 94.4% of patients showed elimination of venous valvular reflux and symptom improvement. In addition to the lack of information on the number of treatments given, the time of patient follow-up was variable (from 1 month to 2 years), precluding any conclusions regarding the durability of the treatment.

Subsection Summary: Sclerotherapy

In a Cochrane review, ultrasound-guided foam sclerotherapy was inferior to ligation and stripping and endovenous laser ablation for technical success up to 5 years and beyond 5 years, but there was no significant difference between treatments for recurrence up to 3 years and at 5 years. For physician-compounded sclerotherapy, there is high variability in success rates of the procedure and

some reports of serious adverse events. Results of a noninferiority trial of physician-compounded sclerotherapy indicated that once occluded, recurrence rates at 2 years are similar to those of ligation and stripping. By comparison, rates of occlusion with the FDA-approved microfoam sclerotherapy (polidocanol 1%) are similar to those reported for endovenous laser ablation or stripping.

Treatment of Saphenous Veins: Mechanochemical Ablation

Randomized Controlled Trials

Four RCTs with over 100 patients each (range, 132 to 213) have been identified that compared MOCA to thermal ablation. Study characteristics and study results are presented in Tables 3 and 4. Study limitations are described in Tables 5 and 6.

Two publications (Bootun et al [2016], Lane et al [2017]) reported on early results from an RCT of 170 patients that compared ClariVein with RFA.[28,29,] Maximum VAS pain scores (out of 100) during the procedure were significantly lower in the MOCA group (median, 15 mm) than in the RFA group (median, 34 mm; p=.003). Average VAS pain scores during the procedure were also modestly lower in the MOCA group (median, 10 mm) than in the RFA group (median, 19.5 mm; p=.003). Occlusion rates, clinical severity scores, disease-specific quality of life, and generic quality of life scores were similar between the groups at 1 and 6 months. Limitations of this study are described in Tables 5 and 6. Only 71% of patients were available for follow-up at 6 months, limiting the evaluation of closure rates at this time point.

Vahaaho et al (2019) reported an RCT that compared MOCA with endovenous thermal ablation (endovenous laser ablation or RFA).[20,] Liquid sclerosant at a concentration of 1.5% was used. Out of 132 patients enrolled, 7 patients were later excluded and 117 (88.6%) attended the 1-year follow-up evaluation. Occlusion of the great saphenous vein was observed in 45 of 55 (82%) of the MOCA group compared to 100% of the endovenous laser ablation and RFA groups (p=.002). Another randomized trial (Lam et al [2016]) reported interim results of a dose-finding study, finding greater closure with the use of polidocanol 2% or 3% (liquid) than with polidocanol 1%.[30,] Therefore, it is uncertain whether the concentration of sclerosant in the study by Vahaaho et al (2019) was optimal (Table 5).

Three percent polidocanol was tested in the Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation (MARADONA) non-inferiority trial reported by Holewijn et al (2019).[31,] Although the study was powered for 400 participants, only 213 patients were randomized before reimbursement for the procedure was suspended. Pain scores in the 14 days after the procedure were slightly lower, but hyperpigmentation was higher. Anatomic failures were significantly greater in the MOCA group at 1 year and approached significance at 2 years; with the note that the study was underpowered for anatomic failures because of the early stoppage of the study. At 1 and 2 years, clinical and quality of life outcomes were similar in the 2 groups.

A fourth RCT reported by Mohamed et al (2020) is the ongoing Randomized Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency (LAMA).[32,] Patients (n=150) were randomized to MOCA with 1.5% sodium tetradecyl sulfate or to endovenous laser ablation. Anatomic success (occlusion) rates were lower in the MOCA group (77%) compared to the endovenous laser ablation group (91%) with no significant difference between the 2 treatments in intraprocedural pain scores. In contrast to the difference in anatomical occlusion rates, clinical severity and quality of life scores were not significantly different between the groups at 1 year follow-up. Follow-up is continuing to evaluate the durability of the treatments.

Table 3. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Booton et al (2016)[28], Lane et al (2017)[29],				170 patients with varicose veins	MOCA	RFA
Vahaaho et al (2019) [20],				132 patients with varicose veins	MOCA with 1.5% polidocanol	Thermal ablation (endovenous laser ablation or RFA)
Holewijn et al (2019)[31], (MARADONA)	EU	4	2012-2015	213 patients with great saphenous vein incompetence and CEAP C2 to C5	MOCA with 2 mL of 3% polidocanol for the first 10 to 15 cm and 1.5% polidocanol for the remainder	RFA
Mohamed et al (2020)[32],(LAMA)	UK	1	2015-2018	150 patients with symptomatic superficial venous incompetence CEAP grades 2 to 6	MOCA (n=75) with 1.5% sodium tetradecyl sulfate	Endovenous laser ablation (n=75)

CEAP: clinical etiologic anatomic pathological; LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation; MOCA: mechanochemical ablation; RCT: randomized controlled trial; RFA: radiofrequency ablation.

Table 4. Summary of Key RCT Results

Study	Pain	Post-procedure Occlusion Rate	Occlusion Rate at Follow-up	Clinical Severity	Clinical Severity at Follow-up		Quality of Life
Booton et al (2016)[28],Lane et al (2017)[29],	During Procedure - VAS		6 mo occlusion rates				
N			71%		71%		
MOCA	10 mm						
RFA	19.5 mm						
p-value	.003	NS	NS	NS	NS		NS
Vahaaho et al (2019)[20],			1 yr		1 yr		
N			117 (88.6%)		117 (88.6%)		
MOCA			45 of 55 (82%)				
Endovascular laser ablation or RFA			100%				
p- value			.002				
Holewijn et al (2019)[31], (MARADONA)	For 14 days after the procedure median (range)	30 day failure rate	1 yr recanalization rate	2 yr recanalization rate	1 yr VCSS	2 yr VCSS	AVVQ improved
N			153 (72%)	157 (73%)	153 (72%)	157 (73%)	
MOCA	0.2 (0.0 to 0.8)	5 (4.9%)	15 (16.5%)	21 (20%)	1.8	1.0	88%
RFA	0.5 (0.2 to 1.3)	1 (1%)	5 (5.8%)	12 (11.7%)	1.7	1.0	89%
p- value	.01	.10	.025	.066	.695	.882	.90

Study	Pain	Post-procedure Occlusion Rate	Occlusion Rate at Follow-up	Clinical Severity	Clinical Severity at Follow-up	Quality of Life
Mohamed et al (2020)[32], (LAMA)	Median (IQR)		Occlusion at 1 yr		VCSS	AVVQ Median (IQR)
N			138 (92%)			
MOCA	15 (9 to 29)		53/69 (77%)			2.0 (0.0 to 5.3)
Endovascular laser ablation	22 (9 to 44)		63/69 (91%)			2.0 (0.0 to 4.8)
p- value	.21		.020		NS	NS

AVVQ: Aberdeen varicose vein questionnaire; IQR: intraquartile range; LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation; MOCA: mechanochemical ablation; NS: not significant; RCT: randomized controlled trial; RFA: radiofrequency ablation; VAS: visual analog scale.; VCSS: venous clinical severity score.

Table 5. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Bootun et al (2016);[28], Lane et al (2017)[29],				1.Primary outcome was pain during the procedure	1. Outcomes only out to 6 mo, which is insufficient to assess durability
Vahaaho et al (2019)[20],	4. Strict inclusion criteria that may not be representative of intended use.	3. The concentration of sclerosant (1.5% polidocanol) may not have been optimal.			1. Outcomes only out to 1 yr, which is insufficient to assess durability
Holewijn et al (2019)[31], (MARADONA)	4. Patients with bilateral reflux were excluded due to dosing limits of polidocanol				
Mohamed et al (2020)[32], (LAMA)					1. Outcomes out to 1 yr, follow-up is continuing

LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 6. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Bootun et al (2016)[28], Lane et al (2017)[29],		1. Patients not blinded to treatment (assessors of duplex ultrasound were blinded)		1. There was high loss to follow-up (76% follow-up at 1 mo and 71% follow-up at 6 mo)		
Vahaaho et al (2019)[20],		1, 2, 3. Patients, surgeons, and assessors were not blinded to treatment				
Holewijn et al (2019)[31], (MARADONA)		1, 2, 3. Patients, surgeons, and assessors were not blinded to treatment			3. Underpowered for anatomic success due to early termination of recruitment	4. Results of noninferiority analysis were not reported
Mohamed et al (2020) [32],(LAMA)		1, 2, 3. Patients, surgeons, and assessors were not blinded to treatment				2. 14-day pain scores were not analyzed by repeated measures ANOVA

ANOVA: analysis of variance; LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b]Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d]Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. s and/or p values not reported; 4.Comparative treatment effects not calculated.

Prospective Cohort Studies

A prospective cohort study that had a 5-year follow-up was reported by Thierens et al (2019).[33,] Study inclusion criteria are described in Table 7. Anatomic and clinical follow-ups were performed at 4 weeks, 6 months, and 1, 3, and 5 years after the procedure (Table 8). With slightly less than half of the participants remaining in the study through 5 years, 79% had freedom from anatomic failure and clinical measures had worsened. Nearly 15% of the recanalizations occurred in the first year, which the authors considered to be due to technical issues when the procedure was initially introduced. For

example, there had been an increase in the concentration of sclerosant over time. It should be noted, however, that the more recent MARADONA trial from the same group of investigators using 3% polidocanol (described above) also saw a rate of recanalization of 16.5% in the first year and 20% in the second year.[31,] Without a control condition, it cannot be determined whether the loss of clinical improvement in this cohort study is due to recanalization or the usual progression of venous disease over time.

Table 7. Summary of Prospective Cohort Study Characteristics

Study	Country	Participants	Treatment Delivery	Follow-Up
Thierens et al (2019)[33,]	Netherlands	C2 to C5 varicose veins, great saphenous vein diameter of 3 to 12 mm and primary great saphenous vein insufficiency determined by duplex ultrasound examination	MOCA with 2% polidocanol as sclerosant	5 yr

MOCA: mechanochemical ablation.

Table 8. Summary of Prospective Cohort Study Results

Outcome Measure	Baseline	1 yr	3 yr	5 yr
Thierens et al (2019)[33,]	n=94	90	71	58
Freedom from anatomic failure (SE)		85.6% (0.033)	80.1% (0.039)	78.7% (0.041)
AVVQ score	8.9	2.3	5.6	6.3
VCSS score	4.0	1.0	1.0	2.0
Clinical improvement		80%	74%	65%

AVVQ: Aberdeen varicose vein questionnaire; SE: standard error; VCSS: venous clinical severity score.

Subsection Summary: Mechanochemical Ablation

MOCA is a combination of liquid sclerotherapy and mechanical abrasion of the lumen. The evidence on MOCA includes 4 RCTs that compared MOCA to thermal ablation with 6 month to 2-year results, and a prospective cohort with follow-up out to 5 years. Results to date have been mixed regarding a reduction in intraprocedural pain, which is a proposed benefit of MOCA compared to thermal ablation procedures. Occlusion rates at 6 months to 2 years in the RCTs indicate lower anatomic success rates compared to thermal ablation, but a difference in clinical outcomes at these early time points has not been observed. Experience with other endoluminal ablation procedures suggests that lower anatomic success in the short term is associated with recanalization and clinical recurrence between 2 to 5 years. The possibility of later clinical recurrence is supported by a prospective cohort study with 5-year follow-up following treatment with MOCA. However, there have been improvements in technique since the cohort study was begun, and clinical progression is frequently observed with venous disease. Because of these limitations, longer follow-up of the more recently conducted RCTs is needed to establish the efficacy and durability of this procedure compared with the criterion standard of thermal ablation.

Treatment of Saphenous Veins: Cyanoacrylate Adhesive

Randomized Controlled Trials

The VenaSeal pivotal study (VeClose), a multicenter noninferiority trial with 222 patients, compared VenaSeal with RFA for the treatment of venous reflux.[34,35,] The pivotal registration study for the VeClose study and follow-up through 36 months have been published. These reports are summarized in Tables 9 and 10. The primary endpoint (the proportion of patients with complete closure of the target great saphenous vein at 3 months measured by ultrasound) was noninferior to RFA, with a 99% closure rate for VenaSeal compared with 96% for RFA. The secondary endpoint (intraoperative pain) was similar for both groups (2.2 on a 10-point scale for VenaSeal vs. 2.4 for RFA ; p=.11).

Ecchymosis at day 3 was significantly lower in the cyanoacrylate group; 67.6% of patients treated with cyanoacrylate had no ecchymosis compared with 48.2% of patients following RFA (p<.01). Scores on the AVVQ and Venous Clinical Severity Score improved to a similar extent in both groups. The mean time to return to work in a prospective cohort of 50 patients reported by Gibson and Ferris (2017) was 0.2 days.[36,]

For the CAC and RFA groups, the complete occlusion rates were 97.2% and 97.0%. Freedom from recanalization was also similar between the 2 groups (p=.08).[37,] Twenty-four month results were reported by Gibson et al (2018), which included 171 patients (87 from CAC and 84 from RFA).[38,] Thirty-six month results were reported by Morrison et al (2019), with follow-up on 146 (66%) patients (72 from CAC and 74 from RFA).[39,] Loss to follow-up was similar in the 2 groups. The complete closure rates for CAC and RFA were 94.4% and 91.9% (p=.005 for non-inferiority), respectively. Recanalization-free survival through 36 months was not statistically different for the 2 groups. No significant device- or procedure-related adverse events were reported for either group.

VariClose CAC was compared with RFA and endovenous laser ablation by Eroglu and Yasim (2018) in an RCT with 525 patients (Table 9).[40,] Periprocedural outcomes showed a shorter intervention time, less pain, and shorter return to work with CAC compared to endovenous thermal ablation (Table 10). There was no significant difference in occlusion rates between the 3 treatments at 6, 12, and 24-month follow-up.

Table 9. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions[2]	
					Active	Comparator
FDA SSED (2015);[34,] Morrison et al (2015, 2017, 2019);[35,41,39,] Gibson et al (2018);[36,][VeClose trial]	US	10	2013-2014	Age ≥21 and ≤70 years with symptomatic[1] great saphenous vein reflux and CEAP C2-C4b great saphenous vein diameter while standing of 3 to 12 mm	108 VenaSeal CAC	114 RFA
Eroglu and Yasim (2018)[40,]	Asia	1	NR	525 patients ≥18 years with incompetence of the great saphenous vein (>5.5 mm in diameter) or small saphenous vein (>4 mm in diameter) and reflux >0.5 sec	175 VariClose CAC	125 RFA and 125 endovenous laser ablation

CAC: cyanoacrylate; CEAP: Clinical Etiology Anatomy Pathophysiology; FDA: Food and Drug Administration; NR: not reported; RCT: randomized controlled trial; RFA: radiofrequency ablation; SSED; Summary of Safety and Effectiveness Data;
[1] One or more of the following symptoms related to the target vein: aching, throbbing, heaviness, fatigue, pruritus, night cramps, restlessness, generalized pain or discomfort, swelling.
[2] Protocol mandated use of compression stockings for 7 days post-procedure

Table 10. Periprocedural Outcomes

Eroglu and Yasim (2018)[40,]	Duration of Procedure min (SD)	Average Periprocedural Pain[1]	2 or More Analgesics Used Daily n (%)	1 Day to Return to Work n (%)	2 Days to Return to Work n (%)	3 or More Days to Return to Work n (%)
N	503	503	456	456	456	456
VariClose	15.3 (2.6)	1 (mild)	105 (62.5)	161 (95.8)	7 (4.2)	0 (0)
RFA	27.3 (7.7)	2 (moderate)	98 (65.8)	75 (50.3)	53 (35.6)	21 (14.1)

Eroglu and Yasim (2018)[40,]	Duration of Procedure min (SD)	Average Periprocedural Pain[1]	2 or More Analgesics Used Daily n (%)	1 Day to Return to Work n (%)	2 Days to Return to Work n (%)	3 or More Days to Return to Work n (%)
Endovenous laser ablation	35.0 (5.2)	2 (moderate)	105 (75.5)	105 (75.5)	24 (17.3)	10 (7.2)
p- value	<.001		.1472	<.0012		

[1]Scale of 1 to 4; [2]overall p-Value
RFA: radiofrequency ablation; SD: standard deviation.

Table 11. Summary of Key RCT Results

Study	Vein Closure[1] n (%)	Vein Closure 12 months n (%)	Vein Closure 24 months n (%)	Vein Closure 36 months n (%) or VCSS	Device Related Event n (%)
FDA SSED (2015)[34,] Morrison et al (2015, 2017, 2019);[35,41,39,]Gibson et al (2018);[36,][VeClose trial]	**3 months**				
N	222	189	171	146	222
VenaSeal	107 (99.1%)[2]	92 (96.7%)	82/86 (95.3%)	68/72 (94.4%)	31 (27%)
RFA	109 (95.6%)[2]	91 (96.8%)	79/84 (94.0%)	68/74 (91.9%)	7 (6%)
Eroglu and Yasim (2018)[40,]	**6 months**			**VCSS at 24 months**	
N		503	456	456	
VariClose	98.1%	94.1%	95.1%	2.7	
RFA	94.7%	92.5%	94.2%	3.7	
Endovenous laser ablation	92.6%	90.9%	91.5%	3.5	
p- value	NS	NS	NS	<.001	

FDA: Food and Drug Administration; NS: not significant; RCT: randomized controlled trial; RFA: radiofrequency ablation; SSED: Summary of Safety and Effectiveness Data; VCSS: venous clinical severity score.
[1]Complete closure defined as Doppler ultrasound showing vein closure along entire treated vein segment with no discrete segments of patency exceeding 5 cm. Central laboratory confirmation.
[2] Used prespecified data imputation method (Last Observation Carried Forward).

Notable limitations of the studies are shown in Tables 12 and 13. The primary limitation of the pivotal study of VenaSeal is the loss to follow-up at 2 and 3 years, although loss to follow-up was similar in the 2 groups. The study by Eroglu and Yasim (2018) had an unequal loss to follow-up after patients were informed of the treatment allocation. Different expectations in the CAC group compared to the control groups may have influenced subjective outcomes. In addition, VariClose is not currently approved for marketing in the U.S.; both CAC products use N-butyl cyanoacrylate.

Table 12. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Morrison et al (2015), [35,]Morrison et al (2017),[41,]Gibson et al (2018)[38,]Morrison et al (2019)[39,] [VeClose trial]					1.Follow-up scheduled to continue to 60 months
Eroglu and Yasim (2018)[40,]		2. This specific cyanoacrylate product is not currently available in the US			

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

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3.Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 13. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[d]	Data Completeness[e]	Power[d]	Statistical[f]
Morrison et al (2015),[35] Morrison et al (2017),[41] Gibson et al (2018)[38] Morrison et al (2019)[39] [VeClose trial]		1, 2, 3. The outcome was assessed by the treating physician and patients were not blinded		1. >20% loss to follow-up		3. Variable reporting of CI and p values
Eroglu and Yasim (2018)[40]		1, 2, 3. Patients were notified of the group assignment a day before the procedure		6. Not intent-to-treat analysis and unequal loss to follow-up. 21 patients did not receive the allocated intervention, 19 of whom were in the control groups		

CI: confidence interval.
The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3.Evidence of selective publication.
[d]Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Interventionis not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. s and/or p values not reported; 4.Comparative treatment effects not calculated.

Prospective Cohort Studies

Eroglu et al (2017) reported closure rates of 94.1% at 30 months in a prospective cohort of 159 patients.[42] Thirty-three-month follow-up was reported by Zierau (2015) for 467 (58.7%) of 795 veins treated at 1 institution in Germany.[43] An inflammatory reddening of the skin was observed at 1 week posttreatment in 11.7% of cases. No permanent skin responses were observed. Of the 467 veins reexamined, the sealing rate was 97.7%. This series had a high loss to follow-up.

Section Summary: Cyanoacrylate Adhesive

Evidence assessing CAC for the treatment of varicose veins and venous insufficiency includes a multicenter noninferiority trial with follow-up through 36 months, an RCT with follow-up through 24

months, and a prospective cohort with 30 months of follow-up. The short-term efficacy of VenaSeal CAC has been shown to be noninferior to RFA at up to 36 months of follow-up. At 24 and 36 months, the study had greater than 20% loss to follow-up, but loss to follow-up was similar in the 2 groups at the long-term follow-up and is not expected to influence comparative results. A second RCT (N=525) with the same active CAC ingredient (N-butyl cyanoacrylate) that is currently available outside of the U.S. found no significant differences in vein closure between CAC and thermal ablation controls at 24 months of follow-up. The CAC procedure and return to work were shorter and pain scores were lower compared to thermal ablation; the subjective pain scores may have been influenced by differing expectations in this study. A prospective cohort reported high closure rates at 30 months. Overall, results indicate that outcomes from CAC are at least as good as thermal ablation techniques, the current standard of care.

Treatment of Saphenous Veins: Cryoablation

Randomized Controlled Trials

Klem et al (2009) reported on a randomized trial that found endovenous cryoablation (n=249) to be inferior to conventional stripping (n=245) for treating patients with symptomatic varicose veins.[37,] Forty-four percent of patients had residual great saphenous vein remaining with cryoablation while 15% had residual vein remaining with conventional stripping. AVVQ scores also showed better results for conventional stripping (score, 11.7) than cryoablation (score, 8.0). There were no differences between groups in 36-Item Short-Form Health Survey summary scores or neural damage (12% in both groups).

Disselhoff et al (2008, 2011) reported on 2- and 5-year outcomes from a randomized trial that compared cryoablation with endovenous laser ablation.[44,45,] Included were 120 patients with symptomatic uncomplicated varicose veins (CEAP class C2) with saphenofemoral incompetence and great saphenous vein reflux. At 10 days after treatment, endovenous laser ablation provided better results than cryoablation with respect to pain scores over the first 10 days (2.9 vs. 4.4), resumption of normal activity (75% vs. 45%), and induration (15% vs. 52%), all respectively. At a 2-year follow-up, freedom from recurrent incompetence was observed in 77% of patients after endovenous laser ablation and in 66% of patients after cryoablation (p= not significant). At 5 years, 36.7% of patients were lost to follow-up; freedom from incompetence and neovascularization were found in 62% of patients treated with endovenous laser ablation and in 51% of patients treated with cryoablation (p= not significant). Neovascularization was more common after cryoablation, but incompetent tributaries were more common after endovenous laser ablation. There were no significant differences between groups in the Venous Clinical Severity Score or AVVQ scores at either the 2 or 5-month follow-up for endovenous laser ablation.

Subsection Summary: Cryoablation

Two RCTs have suggested that cryotherapy is ineffective for treating varicose veins compared with available alternatives.

Tributary Varicosities

Clinical Context and Therapy Purpose

The purpose of ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins in patients who have varicose tributary veins is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who have varicose tributary veins.

Interventions
The therapy being considered is ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins.

Transilluminated powered phlebectomy (TIPP) is an alternative to stab avulsion and hook phlebectomy. This procedure uses 2 instruments: an illuminator, which also provides irrigation, and a resector, which has an oscillating tip and suction pump. Following removal of the saphenous vein, the illuminator is introduced via a small incision in the skin, and tumescence solution (anesthetic and epinephrine) is infiltrated along the course of varicosity. The resector is then inserted under the skin from the opposite direction, and the oscillating tip is placed directly beneath the illuminated veins to fragment and loosen the veins from the supporting tissue. Irrigation from the illuminator is used to clear the vein fragments and blood through aspiration and additional drainage holes. The illuminator and resector tips may then be repositioned, thereby reducing the number of incisions needed when compared with stab avulsion or hook phlebectomy. It has been proposed that TIPP might decrease surgical time, decrease complications such as bruising, and lead to a faster recovery than established procedures.

Comparators
The following therapy is currently being used to treat varicose tributary veins: conservative therapy.

Outcomes
The general outcomes of interest are reductions in symptoms and morbid events, change in disease status, and improvements in quality of life. Follow-up at 6- and 12-months is of interest for ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins to monitor relevant outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Sclerotherapy and Phlebectomy

Systematic Reviews
Early studies established ligation and stripping as the criterion standard for treating saphenofemoral incompetence based on improved long-term recurrence rates, with sclerotherapy used primarily as an adjunct to treat varicose tributaries. A Cochrane review of 28 studies by de Avlia Oliveira et al (2021) concluded that there is low certainty evidence that sclerotherapy is effective and safe compared to placebo for treating cosmetic appearance, persistent symptoms, and quality of life concerns related to varicose veins.[46,] Evidence was limited or lacking for comparisons of foam with liquid sclerotherapy or other substances, and between concentrations of foam. Sclerotherapy and phlebectomy are considered appropriate in the absence of reflux of the saphenous system (e.g., post- or adjunctive treatment to other procedures such as surgery).[47,]

Randomized Controlled Trials
El-Sheikha et al (2014) reported on a small randomized trial of concomitant or sequential (if needed) phlebectomy following endovenous laser ablation for varicose veins.[48,]Quality of life and clinical severity scores were similar between the groups by 1 year, with 16 (67%) of 24 patients in the sequential phlebectomy group receiving a secondary intervention.

The bulk of the literature discussing the role of ultrasound guidance refers to sclerotherapy of the saphenous vein, as opposed to the varicose tributaries. For example, Yamaki et al (2012) reported on a prospective RCT that compared visual foam sclerotherapy plus ultrasound-guided foam sclerotherapy of the great saphenous vein with visual foam sclerotherapy for varicose tributary veins.[49,] Fifty-one limbs in 48 patients were treated with ultrasound-guided foam sclerotherapy plus visual foam sclerotherapy of the varicose tributaries, and 52 limbs in 49 patients were treated with foam sclerotherapy alone. At 6-month follow-up, complete occlusion was found in 23 (45.1%) limbs treated with ultrasound plus visually guided foam sclerotherapy and in 22 (42.3%) limbs treated with visual sclerotherapy alone. Reflux was absent in 30 (58.8%) limbs treated with ultrasound plus visual guidance and in 37 (71.2%) treated with visual guidance alone (p= not significant). The authors noted that, for the treatment of tributary veins in clinical practice, most patients receive a direct injection of foam without ultrasound guidance.

A small proportion of patients may present with tributary varicosities in the absence of saphenous reflux. For example, as reported by Michaels et al (2006), of 1009 patients recruited for an RCT, 64 patients had minor varicose veins without reflux, 34 of whom agreed to be randomized to sclerotherapy or conservative treatment.[50,] At baseline, 92% had symptoms of heaviness, 69% had cosmetic concerns, 53% reported itching, and 30% reported relief of symptoms using compression hosiery. At 1-year follow-up, there was an improvement in clinician-assessment of the anatomic extent of varicose veins, with 85% of patients in the sclerotherapy group showing improvement compared with 29% of patients in the conservative therapy group. Symptoms of aching were milder or eliminated in 69% of the sclerotherapy group and 28% of the group treated with conservative therapy.

Transilluminated Powered Phlebectomy

Systematic Reviews

A meta-analysis by Luebke and Brunkwall (2008) included 5 studies that compared TIPP with conventional surgery.[51,] Results showed a significant advantage of TIPP over the conventional treatment for the number of incisions, mean cosmetic score, and duration of the procedure. However, TIPP also increased the incidence of hematoma and resulted in worse mean pain scores.

Randomized Controlled Trials

Included in the meta-analysis by Luebke and Brunkwall (2008) was an RCT by Chetter et al (2006) that compared TIPP (n=29) with a multiple stab incision procedure (n=33).[52,] A single surgeon performed all but 2 of the procedures, and there was no difference in operating time. Patients treated with TIPP had an average of 5 incisions, compared with 20 for the multiple stab procedure. However, the blinded evaluation revealed that bruising or discoloration was higher for the TIPP group at 1 and 6 weeks post surgery. At 6 weeks after surgery, patients in the TIPP group showed no reductions in pain (-2 points on the Burford Pain Scale), while patients in the multiple stab incision group had a significant reduction in pain scores compared with presurgical baseline (-20 points). Six weeks post-surgery, quality of life measures had improved in the multiple stab incision group but not in the TIPP group. Thus, although TIPP required fewer surgical incisions, in this single-center study, it was associated with longer recovery due to more extensive bruising, prolonged pain, and reduced early postoperative quality of life.

Section Summary: Tributary Varicosities

The evidence on the use of stab avulsion, sclerotherapy, and phlebectomy includes RCTs and systematic reviews of RCTs. The literature has indicated that sclerotherapy is effective for the treatment of tributary veins following occlusion of the saphenofemoral or saphenopopliteal junction and saphenous veins. No studies have been identified comparing RFA or laser ablation of tributary veins with standard procedures (microphlebectomy and/or sclerotherapy). TIPP is effective at removing varicosities; outcomes are comparable with available alternatives such as stab avulsion and hook phlebectomy. However, there is limited evidence that TIPP is associated with more pain,

bruising, discoloration, and a longer recovery, and the current literature does not show an advantage of TIPP over conventional treatment.

Perforator Reflux

Clinical Context and Therapy Purpose

Perforator veins cross through the fascia and connect the deep and superficial venous systems. Incompetent perforating veins were originally treated with an open surgical procedure, called the Linton procedure, which involved a long medial calf incision to expose all posterior, medial, and paramedial perforators. While this procedure was associated with healing of ulcers, it was largely abandoned due to a high incidence of wound complications. The Linton procedure was subsequently modified by using a series of perpendicular skin flaps instead of a longitudinal skin flap to provide access to incompetent perforator veins in the lower part of the leg. The modified Linton procedure may occasionally be used to close incompetent perforator veins that cannot be reached by less invasive procedures.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who have perforator vein reflux.

Interventions

The therapy being considered is ablation with subfascial endoscopic perforator surgery (SEPS) of perforator veins. SEPS is a less invasive surgical procedure for the treatment of incompetent perforators and has been reported since the mid-1980s. Guided by Duplex ultrasound scanning, small incisions are made in the skin, and the perforating veins are clipped or divided by endoscopic scissors. Endovenous ablation of incompetent perforator veins with sclerotherapy, radiofrequency, and laser ablation has also been reported.

Comparators

The following is currently being used to treat perforator vein reflux: conservative therapy or treatment of saphenous veins alone.

Outcomes

The general outcomes of interest are reductions in symptoms and morbid events, change in disease status, and improvements in quality of life. These may be assessed by VAS, AVVQ, and VCSS, along with ulcer healing and recurrence.

Follow-up at 2 years is of interest for ablation (e.g., SEPS) of perforator veins to monitor relevant outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Giannopoulos et al (2022) performed a systematic review of percutaneous treatments for pathologic perforating veins.[53,] Thirty-five studies met the inclusion criteria (5 double-arm studies and 28 single-

arm studies). Endovenous laser ablation (with or without microphlebectomy and/or sclerotherapy) was successful within the first 2 weeks after the procedure in 95% of patients. Success rates for RFA (with or without microphlebectomy) were 91% (95% CI, 75% to 99%). Ultrasound-guided sclerotherapy had a success rate of 70% after multiple sessions (95% CI, 53% to 84%). After 12 months of follow-up, occlusion rates were 89%, 77%, and 83% in the 3 groups, respectively. Limitations of the review include heterogeneity of the interventions in the included studies, including adjuvant therapy that could be provided at the investigator's discretion.

Ho et al (2022) published a systematic review to compare interventions for incompetent perforator veins, including open ligation, SEPS, endovascular laser ablation, ultrasound-guided sclerotherapy, and RFA.[54,] A total of 81 studies (N=7010) were identified, and the overall quality of evidence was low to intermediate. Results demonstrated that in the short term (≤ 1 year), efficacy rates for wound healing were 99.9% for ultrasound-guided sclerotherapy, 72.2% for open ligation, and 96.0% for SEPS. For short-term freedom from wound recurrence, the pooled estimate for SEPS was 91.0%; wound recurrence rates were not reported for other interventions.

A systematic literature review by O'Donnell (2008) indicated there was a lack of evidence on the role of incompetent perforator vein surgery performed in conjunction with superficial saphenous vein surgery.[5,] These conclusions were based on 4 RCTs published since 2000 that compared superficial vein surgery with conservative therapy for advanced chronic venous insufficiency (CEAP classes C5 to C6). The 4 trials included 2 level I (large subject population) and 2 level II (small subject population) studies. Two trials combined surgical treatment of the incompetent perforator veins with concurrent or prior treatment of the superficial saphenous veins; the other 2 treated the great saphenous vein alone. The 2 randomized studies (2004, 2007) in which the great saphenous vein alone was treated (including the ESCHAR trial) showed a significant reduction in ulcer recurrence compared with conservative therapy.[55,56,]

Treatment of the great saphenous vein alone has been reported to improve perforator function. For example, Blomgren et al (2005) showed that reversal of perforator vein incompetence (28 [41%] of 68 previously incompetent perforators) was more common than new perforator vein incompetence (41 [22%] of 183 previously competent perforators) following superficial vein surgery.[57,]O'Donnell (2008) discussed additional (lower quality) evidence to suggest deep venous valvular involvement rather than incompetent perforators in venous insufficiency.[5,] Thus, although incompetence of perforator veins is frequently cited as an important etiologic factor in the pathogenesis of venous ulcer, current evidence does not support the routine ligation or ablation of perforator veins.

Subfascial Endoscopic Perforator Surgery

A Cochrane review by Lin et al (2019) evaluated the efficacy of SEPS for the treatment of venous ulcers.[58,] The authors identified 4 RCTs, 2 compared SEPS plus compression with compression alone (n=208), 1 compared SEPS with the Linton procedure (n=39), and 1 compared SEPS plus saphenous vein surgery with saphenous vein surgery alone (n=75). Results are shown in Table 14. The authors concluded that:

- Compared with compression alone, there was low certainty evidence that SEPS may increase the rate of ulcer healing compared to compression alone, but it was uncertain whether SEPS reduced the rate of ulcer recurrence.
- Compared with the Linton procedure, it was uncertain whether there was a difference in ulcer healing, and very uncertain whether there was a difference in ulcer recurrence. Based on very low certainty evidence, the Linton procedure was possibly associated with more adverse events.
- Compared to saphenous vein surgery alone, it was uncertain whether there was a difference in ulcer healing or the risk of ulcer recurrence. It was uncertain whether SEPS led to an increase in adverse events (very low certainty due to imprecision and risk of reporting bias)

Table 14. Meta-analysis Results

Comparator	Ulcer Healing	Ulcer Recurrence	Adverse Events
Compression alone N	196	208	
Risk ratio (95% CI)	1.17 (1.03 to 1.33)	0.85 (0.26 to 2.76)	
Linton Procedure N	39	39	39
Risk ratio (95% CI)	0.95 (0.83 to 1.09)	0.47 (0.10 to 2.30)	0.04 (0.00 to 0.60)
Saphenous Vein Surgery	22	75	75
Risk ratio (95% CI)	0.96 (0.64 to 1.43)	1.03 (0.15 to 6.91)	2.05 (0.86 to 4.90)

CI: confidence interval.

In a meta-analysis of SEPS for chronic venous insufficiency, Luebke and Brunkwall (2009) concluded that "its use should not be employed routinely and could only be justified in patients with persistent ulceration thought to be of venous origin, and in whom any superficial reflux has already been ablated and postthrombotic changes excluded."[59,] Reviewers also stated that the "introduction of less invasive techniques for perforator vein ablation, such as ultrasound-guided sclerotherapy or radio-frequency ablation, may diminish the role of subfascial endoscopic perforator surgery in the future."

Retrospective Studies

Lawrence et al (2020) reported a multicenter retrospective review of 832 consecutive patients who met criteria and were treated for venous leg ulcers in the U.S.[60,] Of the 832 patients, 187 were managed with compression alone (75% ulcer healing) and 528 received superficial vein treatment after failure of a mean of 23 months of compression. Of the 528, 344 also underwent ablation of an average of 1.8 perforator veins. Techniques included radiofrequency, laser, and sclerotherapy. The ulcer healing rate was 17% higher in patients treated for perforator reflux (68%) in comparison with superficial vein treatment alone (51%; hazard ratio, 1.619 ; 95% CI, 1.271 to 2.063), even though the ulcers were larger at baseline. Perforator vein treatment did not affect recurrence rates in ulcers that had healed. Larger ulcers were associated with reflux in more than 1 level, and deep vein stenting was performed in 95 patients, some in combination with superficial vein treatment and some in combination with both superficial and perforator vein treatment. The ulcer healing rate in patients who underwent all 3 procedures was 87% at 36 months with an ulcer recurrence of 26% at 24 months.

Section Summary: Perforator Reflux

The literature has shown that the routine ligation and ablation of incompetent perforator veins is not necessary for treating varicose veins and venous insufficiency concurrent with superficial vein procedures. However, when combined superficial vein procedures and compression therapy have failed to improve symptoms (i.e., ulcers), treatment of perforator vein reflux may be as beneficial as any alternative (e.g., deep vein valve replacement). Comparative studies are needed to determine the most effective method of ligating and ablating incompetent perforator veins. There is some low quality evidence that SEPS is as effective as the Linton procedure with a reduction in adverse events. Endovenous ablation with specialized laser or RFA probes has been shown to effectively ablate incompetent perforator veins with a potential decrease in morbidity compared with surgical interventions.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 4 physician specialty societies while this policy was under review in 2015. There was no agreement on the need to treat varicose tributaries to improve functional outcomes in the absence of saphenous vein disease. Input was also mixed on the use of mechanochemical ablation and cyanoacrylate adhesive.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Venous Forum et al

In 2020, in response to published reports of potentially inappropriate application of venous procedures, the American Venous Forum, Society for Vascular Surgery, American Vein and Lymphatic Society, and the Society of Interventional Radiology published appropriate use criteria for the treatment of chronic lower extremity venous disease.[61,] Appropriate use criteria were developed using the RAND/UCLA method incorporating best available evidence and expert opinion.

Appropriate use criteria were determined for various scenarios (e.g., symptomatic, asymptomatic, CEAP [Clinical, Etiology, Anatomy and Pathophysiology] class, axial reflux, saphenofemoral junction reflux) for the following:

- Saphenous vein ablation
  - Great saphenous vein
  - Small saphenous vein
  - Accessory great saphenous vein
- Nontruncal varicose veins
- Diseased tributaries associated with saphenous ablation
- Perforator veins
- Iliac vein or inferior vena cava stenting as a first line treatment
- Duplex ultrasound
- Timing and reimbursement.

Treatment of saphenous veins for asymptomatic CEAP class 1 and 2, or symptomatic class 1, was considered to be rarely appropriate or never appropriate, and treatment of symptomatic CEAP class 2, 3, and 4 to 6 without reflux was rated as never appropriate. Based on the 2011 Guidelines from the Society for Vascular Surgery and American Venous Forum (see below), treatment of perforator veins for asymptomatic or symptomatic CEAP class 1 and 2 was considered to be rarely appropriate or never appropriate. Perforator vein treatment was rated as appropriate for CEAP classes 4 to 6, and may be appropriate for CEAP class 3. Except for a recommendation to use endovenous procedures for perforator vein ablation, techniques used to treat veins in these scenarios were not evaluated.

Society for Vascular Surgery, American Vein and Lymphatic Society, and American Venous Forum

The Society for Vascular Surgery and the American Venous Forum (2011) published joint clinical practice guidelines.[62,] Table 15 provides the recommendations.

Table 15. Guidelines on Management of Varicose Veins and Associated Chronic Venous Diseases

Recommendation	Grade[a]	SOR	QOE
Compression therapy for venous ulcerations and varicose veins			
Compression therapy is recommended as the primary treatment to aid healing of venous ulceration	1B	Strong	Moderate
To decrease the recurrence of venous ulcers, ablation of the incompetent superficial veins in addition to compression therapy is recommended	1A	Strong	High

Recommendation	Grade[a]	SOR	QOE
Use of compression therapy for patients with symptomatic varicose veins is recommended	2C	Weak	Low
Compression therapy as the primary treatment if the patient is a candidate for saphenous vein ablation is not recommended	1B	Strong	Moderate
Treatment of the incompetent great saphenous vein			
Endovenous thermal ablation (radiofrequency or laser) is recommended over chemical ablation with foam or high ligation and stripping due to reduced convalescence and less pain and morbidity. Cryostripping is a technique that is new in the United States, and it has not been fully evaluated.	1B	Strong	Moderate
Varicose tributaries			
Phlebectomy or sclerotherapy are recommended to treat varicose tributaries	1B	Strong	Moderate
Transilluminated powered phlebectomy using lower oscillation speeds and extended tumescence is an alternative to traditional phlebectomy	2C	Weak	Low
Perforating vein incompetence			
Selective treatment of perforating vein incompetence in patients with simple varicose veins is not recommended	1B	Strong	Moderate
Treatment of pathologic perforating veins (outward flow of ≥500 ms duration, with a diameter of ≥3.5 mm) located underneath healed or active ulcers (CEAP class C5-C6) is recommended	2B	Weak	Moderate

CEAP: Clinical Etiology Anatomy Pathophysiology; QOE: quality of evidence; SOR: strength of recommendation.
[a] Grading: strong = 1 or weak = 2, based on a level of evidence that is either high quality = A, moderate quality = B, or low quality = C.

The Society for Vascular Surgery, the American Vein and Lymphatic Society (AVLS), and the American Venous Forum published a joint clinical practice guideline in 2022 on management of lower extremity varicose veins.[63,] The guideline will be published in sections; the first part (published in 2022) focuses on duplex scanning and treatment of superficial truncal reflex. The second part of the guideline has not yet been published. Superficial truncal veins are defined as the great saphenous vein, small saphenous vein, anterior accessory great saphenous vein, and posterior accessory great saphenous vein. A summary of the guideline recommendations is provided in Table 16.

Table 16. Summary of Recommended Treatment of Superficial Truncal Reflex

Recommendation	Grade[a]	SOR	QOE
Symptomatic varicose veins and axial reflux			
Reflux in the great or small saphenous vein - superficial venous intervention preferred over long-term compression stockings	1B	Strong	Moderate
Reflux in the anterior accessory or posterior accessory great saphenous vein - superficial venous intervention preferred over long-term compression stockings	2C	Weak	Low
Reflux in the superficial truncal vein - compression therapy suggested for primary treatment	2C	Weak	Low
Reflux in the great saphenous vein - endovenous ablation preferred over high ligation and stripping[b]	1B	Strong	Moderate
Reflux in the small saphenous vein - endovenous ablation preferred over high ligation and stripping[b]	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory great saphenous vein - endovenous ablation (with phlebectomy if needed) over ligation and stripping[b]	2C	Weak	Low
Patients who place a high priority on long-term outcomes (quality of life and recurrence) - laser ablation, radiofrequency ablation, or ligation and stripping over ultrasound-guided foam sclerotherapy	2C or 2B	Weak	Moderate or Low
Symptomatic axial reflux			
Reflux in the great saphenous vein - thermal and nonthermal ablation recommended	1B	Strong	Moderate
Reflux in the small saphenous vein - thermal and nonthermal ablation recommended	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory great saphenous vein - either thermal or nonthermal ablation suggested	2C	Weak	Low
Varicose veins (CEAP class C2)			

Recommendation	Grade[a]	SOR	QOE
Reflux in the great or small saphenous vein - recommend against concomitant initial ablation and treatment of incompetent perforating veins	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory great saphenous vein - recommend against concomitant initial ablation and treatment of incompetent perforating veins	2C	Weak	Low
Persistent or recurrent symptoms after previous complete ablation - treatment of perforating vein incompetence suggested	2C	Weak	Low
Symptomatic reflux and associated varicosities			
Reflux in the great or small saphenous vein - ablation and concomitant phlebectomy or ultrasound-guided foam sclerotherapy recommended	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory great saphenous vein - ablation and concomitant phlebectomy or ultrasound-guided foam sclerotherapy suggested	2C	Weak	Low

CEAP: Clinical Etiology Anatomy Pathophysiology; QOE: quality of evidence; SOR: strength of recommendation.
[a] Grading: strong = 1 or weak = 2, based on a level of evidence that is either high quality = A, moderate quality = B, or low quality = C.
b Ligation and stripping can be performed if endovenous ablation is not feasible.

American Vein and Lymphatic Society

In 2015, the AVLS(previously named the American College of Phlebology) published guidelines on the treatment of superficial vein disease.[64,]

AVLS gave a Grade 1 recommendation based on high quality evidence that compression is an effective method for the management of symptoms, but when patients have a correctable source of reflux, definitive treatment should be offered unless contraindicated. AVLS recommends against a requirement for compression therapy when a definitive treatment is available. AVLS gave a strong recommendation based on moderate quality evidence that endovenous thermal ablation is the preferred treatment for saphenous and accessory saphenous vein incompetence, and gave a weak recommendation based on moderate quality evidence that mechanochemical ablation may also be used to treat venous reflux.

In 2017, AVLS published guidelines on the treatment of refluxing accessory saphenous veins.[38,] The College gave a Grade 1 recommendation based on level C evidence that patients with symptomatic incompetence of the accessory saphenous veins be treated with endovenous thermal ablation or sclerotherapy to reduce symptomatology. The guidelines noted that although accessory saphenous veins may drain into the great saphenous vein before it drains into the common femoral vein, they can also empty directly into the common femoral vein.

National Institute for Health and Care Excellence

In 2013, the NICE updated its guidance on ultrasound-guided foam sclerotherapy for varicose veins. NICE stated that:

> "1.1 Current evidence on the efficacy of ultrasound-guided foam sclerotherapy for varicose veins is adequate. The evidence on safety is adequate, and provided that patients are warned of the small but significant risks of foam embolization (see section 1.2), this procedure may be used with normal arrangements for clinical governance, consent and audit.
> 1.2 During the consent process, clinicians should inform patients that there are reports of temporary chest tightness, dry cough, headaches and visual disturbance, and rare but significant complications including myocardial infarction, seizures, transient ischaemic attacks and stroke."

In 2015, NICE published a technology assessment on the clinical effectiveness and cost-effectiveness of foam sclerotherapy, endovenous laser ablation, and surgery for varicose veins.[65,]

In 2016, NICE revised its guidance on endovenous mechanochemical ablation, concluding that "Current evidence on the safety and efficacy of endovenous mechanochemical ablation for varicose veins appears adequate to support the use of this procedure...."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 17.

Table 17. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05633277	Outcomes of Sclerotherapy of the Ulcer Bed Compared to a Combination of Ablation and Injections	30	Mar 2024
		180	Dec 2021
NCT04737941	Finnish Venous Ulcer Study	248	Mar 2026
NCT03820947[a]	Global, Post-Market, Prospective, Multi-Center, Randomized Controlled Trial of the VenaSeal™ Closure System vs. Surgical Stripping or Endothermal Ablation (ETA) for the Treatment of Early & Advanced Stage Superficial Venous Disease	500	Apr 2028
Unpublished			
NCT03392753	Randomised Controlled Trial of Mechanochemical Ablation Versus Cyanoacrylate Adhesive for the Treatment of Varicose Veins	167	Dec 2021
NTR4613[a]	Mechanochemical endovenous ablation versus radiofrequency ablation in the treatment of primary small saphenous vein insufficiency (MESSI trial)	160	Apr 2020

NCT: national clinical trial. NTR: Netherlands Trial Registry.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - All prior varicose vein treatments to date and response (including conservative management)
  - Each Leg and each vein to be treated
  - Reason for varicose vein treatment
  - Type of treatment/procedure requested for each vein in each leg
  - Documentation of Doppler and/or Duplex ultrasounds showing reflux
  - For additional treatments not done on the original date of service, documentation why they were not treated initially and/or why they need treatment now

Post Service (in addition to the above, please include the following):

- Varicose vein treatment operative/procedure report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0524T	Endovenous catheter directed chemical ablation with balloon isolation of incompetent extremity vein, open or percutaneous, including all

Type	Code	Description
		vascular access, catheter manipulation, diagnostic imaging, imaging guidance and monitoring
	36465	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; single incompetent extremity truncal vein (great saphenous vein, accessory saphenous vein)
	36466	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; multiple incompetent truncal veins (great saphenous vein, accessory saphenous vein), same leg
	36468	Injection(s) of sclerosant for spider veins (telangiectasia), limb or trunk
	36470	Injection of sclerosant; single incompetent vein (other than telangiectasia)
	36471	Injection of sclerosant; multiple incompetent veins (other than telangiectasia), same leg
	36473	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated
	36474	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)
	36475	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated
	36476	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
	36478	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated
	36479	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
	36482	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; first vein treated
	36483	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
	37500	Vascular endoscopy, surgical, with ligation of perforator veins, subfascial (SEPS)
	37700	Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions
	37718	Ligation, division, and stripping, short saphenous vein

Type	Code	Description
	37722	Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below
	37735	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 le.g., with excision of deep fascia
	37760	Ligation of perforator veins, subfascial, radical (Linton type), including skin graft, when performed, open,1 leg
	37761	Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg
	37765	Stab phlebectomy of varicose veins, 1 extremity; 10-20 stab incisions
	37766	Stab phlebectomy of varicose veins, 1 extremity; more than 20 incisions
	37780	Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)
	37785	Ligation, division, and/or excision of varicose vein cluster(s), 1 leg
	37799	Unlisted procedure, vascular surgery
	76942	Ultrasonic guidance for needle placement (biopsy, aspiration, injection, localization device), imaging supervision and interpretation
	93970	Duplex scan of extremity veins including responses to compression and other maneuvers; complete bilateral study
	93971	Duplex scan of extremity veins including responses to compression and other maneuvers; unilateral or limited study
HCPCS	S2202	Echosclerotherapy

Policy History

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

Effective Date	Action
10/11/2000	New Policy Adoption
02/26/2002	Coding Update
10/29/2002	Coding Update
09/01/2003	Policy Revision
05/01/2006	Policy Revision
08/01/2006	Policy Revision
06/28/2007	BCBSA Medical Policy adoption
12/10/2008	Policy Title Revision, criteria revised, BCBSA Medical Policy Adoption
09/03/2009	Administrative Review
07/01/2011	Policy revision with position change
01/30/2015	Policy title change from Varicose Vein Treatments Policy revision with position change effective 03/30/2015
03/30/2015	Policy revision with position change Coding update
09/01/2016	Policy revision without position change
02/01/2017	Policy revision without position change Coding update
07/01/2017	Policy revision without position change
02/01/2018	Coding update
07/01/2018	Policy revision without position change
02/01/2019	Policy Guidelines clarification

Effective Date	Action
	Coding update
04/01/2019	Policy revision without position change
09/01/2019	Policy revision with position change
05/01/2020	Administrative update. Policy statement and guidelines updated.
08/01/2020	Annual review. Policy statement, guidelines and literature updated.
07/01/2021	Annual review. No change to policy statement. Literature review updated.
11/01/2021	Coding update
07/01/2022	Annual review. Policy statement, guidelines and literature updated.
07/01/2023	Annual review. Policy statement, guidelines and literature updated.
09/01/2023	Administrative update.
12/01/2023	Policy statement and guidelines updated.
03/01/2024	Annual review. Policy statement updated.
05/01/2024	Administrative update.

Definitions of Decision Determinations

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

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue

Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Treatment of Varicose Veins/Venous Insufficiency 7.01.124 **Policy Statement:** **Great, Small, or Accessory Saphenous Veins** I. Saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met: A. Documentation to use **only one** of the following procedures (not combined use of different procedures or an unlisted procedure): surgery (ligation and stripping), radiofrequency endovenous thermal ablation, laser endovenous thermal ablation, microfoam sclerotherapy, or cyanoacrylate adhesion B. There is demonstrated saphenous reflux and CEAP (Clinical, Etiology, Anatomy, Pathophysiology) class C2 or greater C. There is documentation of **one or more** of the following: 1. Ulceration secondary to venous stasis 2. Recurrent superficial thrombophlebitis 3. Hemorrhage or recurrent bleeding episodes from a ruptured superficial varicosity 4. Persistent pain, swelling, itching, burning, or other symptoms are associated with saphenous reflux, and **both** of the following: a. The symptoms significantly interfere with activities of daily living b. Conservative management including compression therapy for at least 6 weeks has not improved the symptoms II. Treatment of saphenous veins by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy or cyanoacrylate adhesive that does not meet the criteria described above is considered **investigational**. III. Combining the use of **any two** medically necessary treatments (radiofrequency ablation [RFA] and microfoam sclerotherapy) during	**Treatment of Varicose Veins/Venous Insufficiency 7.01.124** **Policy Statement:** **Great, Small, or Accessory Saphenous Veins** I. Saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met: A. Documentation to use **only one** of the following procedures (not combined use of different procedures or an unlisted procedure): surgery (ligation and stripping), radiofrequency endovenous thermal ablation, laser endovenous thermal ablation, microfoam sclerotherapy, or cyanoacrylate adhesion B. There is demonstrated saphenous reflux and CEAP (Clinical, Etiology, Anatomy, Pathophysiology) class C2 or greater C. There is documentation of **one or more** of the following: 1. Ulceration secondary to venous stasis 2. Recurrent superficial thrombophlebitis 3. Hemorrhage or recurrent bleeding episodes from a ruptured superficial varicosity 4. Persistent pain, swelling, itching, burning, or other symptoms are associated with saphenous reflux, and **both** of the following: a. The symptoms significantly interfere with activities of daily living b. Conservative management including compression therapy for at least 6 weeks has not improved the symptoms II. Treatment of saphenous veins by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy or cyanoacrylate adhesive that does not meet the criteria described above is considered **investigational**. III. Combining the use of **any two** medically necessary treatments (radiofrequency ablation [RFA] and microfoam sclerotherapy) during

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
the same treatment session on the same vein or same type of vein is considered **not medically necessary**.	the same treatment session on the same vein or same type of vein is considered **not medically necessary**.
IV. Sclerotherapy techniques (other than microfoam sclerotherapy) as the primary treatment of great, small, or accessory saphenous veins, is considered **investigational.** However, standard foam sclerotherapy can be used for cleanup of small sections of saphenous veins when needed after primary treatment by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, or cyanoacrylate adhesive.	IV. Sclerotherapy techniques (other than microfoam sclerotherapy) as the primary treatment of great, small, or accessory saphenous veins, is considered **investigational.** However, standard foam sclerotherapy can be used for cleanup of small sections of saphenous veins when needed after primary treatment by surgery, endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, or cyanoacrylate adhesive.
V. Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy of perforator, great, small, or accessory saphenous veins are considered **investigational.**	V. Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy of perforator, great, small, or accessory saphenous veins are considered **investigational.**
Symptomatic Varicose Tributaries	**Symptomatic Varicose Tributaries**
VI. Tributary varicosity treatment when performed either at the same time (or following prior treatment) as saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met: A. Documentation to use **one** of the following procedures (not an unlisted procedure): stab avulsion, hook phlebectomy, standard sclerotherapy (not including microfoam sclerotherapy), transilluminated powered phlebectomy B. Saphenous veins have been previously treated successfully or will be treated during the same session C. The tributaries are symptomatic D. All tributaries in the same leg meeting criteria for treatment will be treated in the same session (or have documentation submitted when that should not be done) E. Use of microfoam sclerotherapy or cyanoacrylate only when using leftover product during the same session as saphenous vein treatments using the same agent	VI. Tributary varicosity treatment when performed either at the same time (or following prior treatment) as saphenous vein treatment may be considered **medically necessary** when **all** of the following criteria have been met: A. Documentation to use **one** of the following procedures (not an unlisted procedure): stab avulsion, hook phlebectomy, standard sclerotherapy (not including microfoam sclerotherapy), transilluminated powered phlebectomy B. Saphenous veins have been previously treated successfully or will be treated during the same session C. The tributaries are symptomatic D. All tributaries in the same leg meeting criteria for treatment will be treated in the same session (or have documentation submitted when that should not be done) E. Use of microfoam sclerotherapy or cyanoacrylate only when using leftover product during the same session as saphenous vein treatments using the same agent
VII. When done separately from saphenous vein treatment, the use of microfoam sclerotherapy (does NOT apply to standard foam	VII. When done separately from saphenous vein treatment, the use of microfoam sclerotherapy (does NOT apply to standard foam

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
sclerotherapy) or cyanoacrylate to treat symptomatic varicose tributaries is considered to be **investigational**, either: A. On a different date as saphenous vein treatment B. On the same date when saphenous vein treatment was done using a different modality (i.e., RFA, laser or surgery)	sclerotherapy) or cyanoacrylate to treat symptomatic varicose tributaries is considered to be **investigational**, either: A. On a different date as saphenous vein treatment B. On the same date when saphenous vein treatment was done using a different modality (i.e., RFA, laser or surgery)
VIII. The following are considered **investigational**: A. Treatment of isolated tributary veins without prior or concurrent treatment of saphenous veins B. Isolated treatment of symptomatic varicose tributaries using any other techniques than those noted above C. Endovenous radiofrequency or laser ablation of tributary veins	VIII. The following are considered **investigational**: A. Treatment of isolated tributary veins without prior or concurrent treatment of saphenous veins B. Isolated treatment of symptomatic varicose tributaries using any other techniques than those noted above C. Endovenous radiofrequency or laser ablation of tributary veins
Perforator Veins IX. Perforator vein treatments for leg ulcers may use surgical ligation (including Subfascial Endoscopic Perforator Surgery-SEPS) or endovenous thermal ablation (radiofrequency or laser), microfoam or standard foam sclerotherapy or cyanoacrylate adhesion may be considered **medically necessary** when **all** of the following conditions have been met: A. There is demonstrated perforator reflux B. Any superficial saphenous veins (great, small, or accessory saphenous and symptomatic varicose tributaries) have been previously eliminated C. Ulcers are present that have not resolved following combined superficial vein treatment and compression therapy for at least 3 months D. The venous insufficiency is not secondary to deep venous thromboembolism	**Perforator Veins** IX. Perforator vein treatments for leg ulcers may use surgical ligation (including Subfascial Endoscopic Perforator Surgery-SEPS) or endovenous thermal ablation (radiofrequency or laser), microfoam or standard foam sclerotherapy or cyanoacryolate adhesion may be considered **medically necessary** when **all** of the following conditions have been met: A. There is demonstrated perforator reflux B. Any superficial saphenous veins (great, small, or accessory saphenous and symptomatic varicose tributaries) have been previously eliminated C. Ulcers are present that have not resolved following combined superficial vein treatment and compression therapy for at least 3 months D. The venous insufficiency is not secondary to deep venous thromboembolism
X. Stab avulsion, hook phlebectomy, transilluminated powered phlebectomy of perforator veins are considered **investigational.**	X. Stab avulsion, hook phlebectomy, transilluminated powered phlebectomy of perforator veins are considered **investigational.**
Telangiectasia XI. Treatment of telangiectasia such as spider veins, angiomata, and hemangiomata that are less than 3 millimeters in diameter are considered **investigational**.	**Telangiectasia** XI. Treatment of telangiectasia such as spider veins, angiomata, and hemangiomata that are less than 3 millimeters in diameter are considered **investigational**.

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Miscellaneous XII. The following are considered **investigational**: A. Mechanochemical ablation (MOCA) of any vein B. Endovenous cryoablation of any vein	**Miscellaneous** XII. The following are considered **investigational**: A. Mechanochemical ablation (MOCA) of any vein B. Endovenous cryoablation of any vein