Title: Varicose Veins

Professional
Original Effective Date: January 1, 2004
Revision Date(s): August 17, 2004; August 24, 2004; May 19, 2005; December 15, 2005; February 17, 2006; October 10, 2006; October 31, 2006; February 6, 2007; September 7, 2007; October 16, 2007; January 4, 2008; July 18, 2008, April 22, 2009; November 18, 2009; January 1, 2010; October 11, 2010; May 4, 2011; September 6, 2011; September 11, 2012; March 8, 2013; December 24, 2014; January 1, 2016; February 1, 2019; September 13, 2019
Current Effective Date: September 13, 2019

Institutional
Original Effective Date: April 22, 2009
Revision Date(s): November 18, 2009; January 1, 2010; October 11, 2010; May 4, 2011; September 6, 2011; September 30, 2011; October 11, 2012; March 8, 2013; December 24, 2014; January 1, 2016; February 1, 2019; September 13, 2019
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### Populations
- Individuals: With varicose veins/venous insufficiency and saphenous vein reflux
  - Interventions of interest are: Microfoam sclerotherapy
  - Comparators of interest are: Conservative therapy, Ligation and stripping, Endovenous radiofrequency or laser ablation
  - Relevant outcomes include: Symptoms, Change in disease status, Morbid events, Quality of life, Treatment-related morbidity

### Interventions
- Individuals: With varicose veins/venous insufficiency and saphenous vein reflux
  - Comparators of interest are: Conservative therapy, Ligation and stripping, Endovenous radiofrequency or laser ablation
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  - Relevant outcomes include: Symptoms, Change in disease status, Morbid events, Quality of life, Treatment-related morbidity

- Individuals: With varicose tributary veins
  - Interventions of interest are: Ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins
  - Comparators of interest are: Conservative therapy
  - Relevant outcomes include: Symptoms, Change in disease status, Morbid events, Quality of life, Treatment-related morbidity

- Individuals: With perforator vein reflux
  - Interventions of interest are: Ablation (eg, subfascial endoscopic perforator surgery) of perforator veins
  - Comparators of interest are: Conservative therapy
  - Relevant outcomes include: Symptoms, Change in disease status, Morbid events, Quality of life, Treatment-related morbidity

### Description
A variety of treatment modalities are available to treat varicose veins / venous insufficiency, including surgery, thermal ablation, and 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) treatments.

### Objective
The objective of this evidence review is to evaluate whether the use of ablative, chemical, and adhesive technologies to treat varicose veins/venous insufficiency arising from reflux in the saphenous, tributary, and perforator veins improves net health outcomes.
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 (CEAP) characteristics of venous insufficiency, ranging from class 0 (no visible sign of disease) to class 6 (active ulceration):

Definitions
Varicose Veins are dilated, elongated, tortuous, subcutaneous veins three millimeters or greater in size.

Telangiectases (i.e. spider veins, spider burst, web veins, thread veins, dilated venules) are permanently dilated blood vessels less than 1 mm in diameter.

Reticular Veins are abnormal dilations of the normal plexuses venosus appearing as a bluish or greenish net and are usually 2-4 mm in diameter.

Venulectasias are bluish vessels sometimes distended above the skin surface and most often 1-2 mm in diameter.

Treatment
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 in 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
and small saphenous veins are eliminated, and blood flow is diverted through the accessory veins.

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 typically includes the following:

1. Identification by preoperative Doppler ultrasonography of the valvular incompetence
2. Control of the most proximal point of reflux, traditionally by suture ligation of the incompetent saphenofemoral or saphenopopliteal junction
3. Removal of the superficial vein from circulation, eg, by stripping of the great and/or small saphenous veins
4. 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. They include sclerotherapy, transilluminated powered phlebectomy (TIPP), and thermal ablation using cryotherapy, high-frequency radio waves (200–300 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 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 commonly produced by forcibly mixing a gas (eg, air or carbon dioxide) with a liquid sclerosant (eg, polidocanol or sodium tetradecyl sulfate). Physician-compounded foam is produced at the time of treatment.
commercially available microfoam sclerosant with a proprietary gas mix is available that is proposed to provide 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 3,500 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 need for the tumescent anesthesia used with endovenous thermal ablation techniques (radiofrequency ablation [RFA], endovenous laser ablation.

**Cyanoacrylate Adhesive**
A cyanoacrylate adhesive is a clear, free-flowing liquid that polymerizes in the vessel via an anionic mechanism (ie, 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 (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 the 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.
Treatment of Perforator Veins
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.

Subfascial endoscopic perforator surgery (SEPS) is a less invasive surgical procedure for 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. The surgery can be performed as an outpatient procedure. Endovenous ablation of incompetent perforator veins with sclerotherapy and RFA has also been reported.

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 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 FDA through the 501(k) process for endovenous treatment of superficial vein reflux:
- In 1999, the VNUS Closure™ System, a radiofrequency device, was cleared by FDA through the 510(k) process for "endovascular coagulation of blood vessels in patients with superficial vein reflux." In 2005, the VNUS RFS™ and RFSFlex™ devices were cleared by the FDA for "use in vessel and tissue coagulation including treatment of incompetent (ie, refluxing) perforator and tributary veins." In 2008, the modified VNUS ClosureFast™ Intravascular Catheter was cleared by 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 was 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. 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 (Vascular Insights) 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.
POLICY

I. SAPHENOUS VEINS - Great-or Small Saphenous Veins

A. Treatment of the great or small saphenous veins by surgery (ligation and stripping) endovenous thermal ablation (radiofrequency or laser), or microfoam sclerotherapy may be considered medically necessary for symptomatic varicose veins / venous insufficiency when all the following criteria have been met:

1. There is demonstrated saphenous reflux and CEAP [Clinical, Etiology, Anatomy, Pathophysiology], class C2 or greater

   AND

2. There is documentation of 1 or more of the following indications:
   a. Ulceration secondary to venous stasis
      OR
   b. Recurrent superficial thrombophlebitis
      OR
   c. Hemorrhage or recurrent bleeding episodes from a ruptured superficial varicosity
      OR
   d. All of the following:
      1) Persistent pain, swelling, itching, burning, or other symptoms associated with saphenous reflux
         AND
      2) the symptoms significantly interfere with activities of daily living
         AND
      3) conservative management including compression therapy for at least 3 months has not improved the symptoms

B. Treatment of great or small saphenous veins by surgery, endovenous thermal ablation (radiofrequency or laser), or microfoam sclerotherapy that does not meet the criteria described above is considered not medically necessary.

C. Treatment of the great or small saphenous veins by cyanoacrylate adhesive is considered not medically necessary for symptomatic varicose veins / venous insufficiency (see Policy Guideline 1).

D. Treatment of varicose veins for cosmetic purposes is not covered.
II. ACCESSORY SAPHENOUS VEINS

A. Treatment of accessory saphenous veins by surgery (ligation and stripping), endovenous thermal ablation (radiofrequency or laser) or microfoam sclerotherapy may be considered **medically necessary** for symptomatic varicose veins / venous insufficiency when all the following criteria have been met:

1. One of the following:
   a. Incompetence of the accessory saphenous vein, when documentation of the anatomy supports the reflux is isolated
   OR
   b. The great or small saphenous veins had been previously eliminated (at least 3 months)

   **AND**

2. There is demonstrated accessory saphenous reflux

   **AND**

3. There is documentation of 1 or more of the following indications:
   a. Ulceration secondary to venous stasis
   OR
   b. Recurrent superficial thrombophlebitis
   OR
   c. Hemorrhage or recurrent bleeding episodes from a ruptured superficial varicosity
   OR
   d. All of the following:
      1) Persistent pain, swelling, itching, burning, or other symptoms associated with saphenous reflux
      **AND**
      2) the symptoms significantly interfere with activities of daily living
      **AND**
      3) conservative management including compression therapy for at least 3 months has not improved the symptoms

B. Treatment of accessory saphenous veins by surgery, endovenous thermal ablation (radiofrequency or laser), or microfoam sclerotherapy that do not meet the criteria described above is considered **not medically necessary**.

C. Treatment of accessory saphenous veins by cyanoacrylate adhesive is considered **not medically necessary** for symptomatic varicose veins / venous insufficiency (see Policy Guideline 1).

D. Treatment of varicose veins for cosmetic purposes is **not covered**.
III. SYMPTOMATIC VARICOSE TRIBUTARIES
   A. When physical findings support medical necessity; the following treatments are considered **medically necessary** as a component of the treatment of symptomatic varicose tributaries (none of these techniques has been shown to be superior to another):
      1. Stab avulsion
      2. Hook phlebectomy
      3. Sclerotherapy
      4. Transilluminated powered phlebectomy

   B. The sole treatment of varicose vein tributaries in the presence of saphenofemoral or saphenopopliteal reflux is considered **not medically necessary**.

   C. Treatment of tributary veins less than 3 mm is considered **cosmetic and not covered**.

IV. PERFORATOR VEINS
   A. Surgical ligation (including subfascial endoscopic perforator surgery) or endovenous thermal ablation (radiofrequency or laser) of incompetent perforator veins may be considered **medically necessary** as a treatment of leg ulcers associated with chronic venous insufficiency when all the following conditions have been met:
      1. There is demonstrated perforator reflux
         **AND**
      2. The superficial saphenous veins (great, small, or accessory saphenous and symptomatic varicose tributaries) have been previously eliminated
         **AND**
      3. Ulcers have not resolved following combined superficial vein treatment and compression therapy for at least 3 months
         **AND**
      4. The venous insufficiency is not secondary to deep venous thromboembolism
B. Treatment of incompetent perforator veins without refractory stasis ulceration is considered not medically necessary as discussed in reference 5:
1. "Patients with isolated reflux in perforator veins...are generally asymptomatic; reflux at multiple valve sites is required for symptom expression."
2. "Reflux in perforator veins that are smaller than 4mm in diameter is not considered to be clinically significant.
3. "In complex venous disease, comprehensive correction is neither feasible nor necessary; partial correction of multifocal disease often relieves symptoms."
4. "The role of interruption of the perforator vein is controversial because of doubts about the pathologic significance of reflux involving this vein and because its specific efficacy is uncertain."
5. "The role of perforator vein ablation awaits results of properly conducted randomized controlled trials."
6. Perforator reflux often resolves following saphenous ablation.

C. Ligation or ablation of incompetent perforator veins performed concurrently with superficial venous surgery is not medically necessary.

V. Telangiectasia
Treatment of telangiectasia such as spider veins, angiomata, and hemangiomata is considered cosmetic and not covered.

VI. Other Veins
A. Techniques for conditions not specifically listed above are experimental / investigational including, but not limited to:
1. Sclerotherapy techniques, other than microfoam sclerotherapy, of great, small, or accessory saphenous veins
2. Sclerotherapy of perforator veins
3. Sclerotherapy of isolated tributary veins without prior or concurrent treatment of saphenous veins
4. Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy of perforator, great or small saphenous, or accessory saphenous veins.
5. Endovenous radiofrequency or laser ablation of tributary veins
6. Mechanochemical ablation of any vein
7. Endovenous cryoablation of any vein
Policy Guidelines
1. For a service to be considered medically necessary, it should not be more costly than an alternative service or supply or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results for the illness, injury, or disease.

2. 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

<table>
<thead>
<tr>
<th>Class</th>
<th>Definition</th>
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<tbody>
<tr>
<td>C0</td>
<td>No visible or palpable signs of venous disease</td>
</tr>
<tr>
<td>C1</td>
<td>Telangiectasies or reticular veins</td>
</tr>
<tr>
<td>C2</td>
<td>Varicose veins</td>
</tr>
<tr>
<td>C3</td>
<td>Edema</td>
</tr>
<tr>
<td>C4a</td>
<td>Pigmentation and eczema</td>
</tr>
<tr>
<td>C4b</td>
<td>Lipodermatosclerosis and atrophie blanche</td>
</tr>
<tr>
<td>C5</td>
<td>Healed venous ulcer</td>
</tr>
<tr>
<td>C6</td>
<td>Active venous ulcer</td>
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<tr>
<td>S</td>
<td>Symptoms including ache, pain, tightness, skin irritation, heaviness, muscle cramps, as well as other complaints attributable to venous dysfunction</td>
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<tr>
<td>A</td>
<td>Asymptomatic</td>
</tr>
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3. A clear and complete description of the physical exam of the lower extremities that documents the medical necessity of treatment for venous insufficiency for medical, not cosmetic purposes, is required. Physical findings that support medically significant venous hypertension must be clearly documented. Treatment of varicose veins for cosmetic purposes is not covered. Photographs may be requested.

4. Up to 20 injections in each leg may be treated in any one session and up to 3 sclerotherapy sessions for each leg may be considered medically necessary if selection criteria are met.

5. Following successful ablation of the greater saphenous vein, tributary veins can become more prominent, but usually improve over time; therefore, delaying treatment of these smaller veins will minimize the number of veins that need treatment.

6. Patients with combined deep and superficial venous insufficiency are often not good candidates for ablation therapy. Varicose vein recurrence and ulcer recurrence rates following intervention are much higher. However, deep vein insufficiency is not a contraindication to superficial vein treatment.
7. It should be noted that the bulk of the literature discussing the role of ultrasound guidance refers to sclerotherapy of the saphenous vein, as opposed to the varicose tributaries. When ultrasound guidance is used to guide sclerotherapy of the varicose tributaries, it would be considered either not medically necessary or incidental to the injection procedure.

Claims Submission Instructions
1. CPT code 36470 should be used when only one vein is injected on a given date of service.
2. CPT code 36471 should be used when more than one vein in the same leg is injected on a given date of service.
3. If both legs are injected, right and left modifier should be used on claims with the codes to indicate which leg is being treated. The following coding conventions should be used:
   - One vein on the left; two veins on the right: 36470 LT and 36471 RT. Injections for each leg should be reported on a separate line.
   - One vein on each leg: Use 36470 RT and 36470 LT.
   - Two veins on the right; three on the left: 36471 RT and 36471 LT.
   - In each case, the correct quantity to bill is one unit per code.
4. For less than 10 phlebectomies, CPT code 37799 should be used, modifier 22 added and box 19 of the claim form populated with "phlebectomies less than 10".

Reimbursement
1. The use of the following ultrasound guidance procedures (76937, 76942, 76998, 76999, 93965, 93970, 93971, S2202) during varicose vein surgery is considered content of service.
2. CPT codes 93965, 93970 or 93971 Doppler ultrasound should not be billed for intraoperative procedures. If these codes are billed separately as the initial diagnostic tool for mapping, the claim will be allowed if medically necessary. Any additional scans over the initial mapping may be reviewed for medical necessity.
3. Selective catheter placement is content of service of a covered procedure.
4. Reimbursement for sclerotherapy will be limited to 3 sessions.

RATIONALE
This evidence review has been updated with searches of the MEDLINE database. The most recent literature update was performed through March 26, 2019.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or
worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

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.

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 (ie, ligation and stripping) compared with compression therapy.

**Conventional Treatment of Saphenous Reflux Compression Therapy**

A Cochrane review by O’Meara et al (2009) evaluated compression for venous leg ulcers included 39 RCTs with 47 different comparisons. This review was updated in 2012 and included 48 RCTs with 59 different comparisons. 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 eight 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 the mean time to ulcer healing was approximately two months, while the median time to healing in other reports was three to five months.

A Cochrane review by Shingler et al (2011) assessed compression stockings as initial treatment for varicose veins in patients without venous ulceration. Selected were 7 studies involving 356 participants with varicose veins without healed or active venous ulceration (CEAP [Clinical, Etiology, Anatomy, Pathophysiology] class C2-C4). Six studies compared different types or pressures of stockings. Subjectively, participants symptoms improved, but results were not
compared with a control arm. Due primarily to inadequate reporting, the methodologic quality of the selected trials was unclear. Meta-analyses were not performed due to inadequate reporting and suspected heterogeneity. 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. 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. 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. At 2 years, Doppler ultrasound demonstrated reflux in approximately 10% of patients after ligation and stripping, increasing to 15% at 3 years.

Treatment of Saphenous Veins
Clinical Context and Therapy Purpose
The purpose of endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, mechanochemical ablation, cyanoacrylate adhesive, or cryoablation in patients 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 therapies.

The question addressed in this evidence review is: Does the use of endovenous thermal ablation (radiofrequency or laser), microfoam sclerotherapy, mechanochemical ablation, cyanoacrylate adhesive, or cryoablation improve the net health outcome in individuals who have varicose veins/venous insufficiency and saphenous vein reflux?

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

Patients
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, mechanochemical ablation, cyanoacrylate adhesive, 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 (mechanochemical ablation MOCA],
cyanoacrylate adhesive CAC] and cryotherapy) do not require tumescent anesthesia are now
compared with the thermal ablation procedures.

Outcomes
The general outcomes of interest for all five interventions are reductions in symptoms and
morbid events, change in disease status, and improvements in QOL. Specific measures may
include the visual analog score for pain, the Varicose Vein Severity Score, and the Aberdeen
Varicose Veins Questionnaire (AVVQ). AVVQ scores range from 0 to 100 (worst possible quality of
life). Follow-up at one and two years from RCTs is of interest to monitor treatment success (vein
occlusion and recanalization), with follow-up to five years to assess durability of the treatment.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with
   a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a
   preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer
   periods of follow up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Treatment of Saphenous Veins: Endovenous Thermal Ablation (laser or radiofrequency)
Systematic Reviews
A Cochrane review by Nesbitt et al (2014) compared endovenous ablation (radiofrequency and
laser) with foam sclerotherapy or ligation and stripping for saphenous vein varices.8, Included in
the review were 13 randomized studies (total n=3081 patients). The overall quality of the
evidence was moderate. There was no significant difference between sclerotherapy and surgery
in the rate of recurrence, as rated by clinicians (odds ratio [OR], 1.74; p=0.06) or for
symptomatic recurrence (OR=1.28). For endovenous laser ablation vs surgery, there were no
significant differences between the treatment groups for clinician-reported or symptomatic
recurrence, or for recanalization. Neovascularization and technical failure were reduced in the
laser group (OR=0.05, p<0.001; OR=0.29, p<0.001, respectively). For endovenous
radiofrequency ablation (RFA) vs surgery, there were no significant differences between groups
in clinician-reported recurrence, recanalization, neovascularization, or technical failure. Reviewers
concluded that sclerotherapy, endovenous laser ablation, and RFA are at least as effective as
surgery in the treatment of great saphenous varicose veins.

A Cochrane review by Paravastu et al (2016) compared endovenous laser ablation or RFA with
surgical repair for short saphenous veins with reflux at the saphenopopliteal junction.9, 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% confidence interval [CI], 0.02 to
0.22), and low-quality evidence that recurrence of reflux was lower after endovenous laser
ablationat 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. 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 QOL 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 Comparable effectiveness of endovenous laser ablation and high ligation with 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. At two-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 QOL. Saphenofemoral reflux was detected by ultrasonography more frequently after endovenous laser treatment (17.8% vs 1.3%). The follow-up rate at five years was 81%. Same-site recurrences were more frequent in the endovenous laser ablation group (18% with endovenous laser ablation vs 5% with surgery, p=0.002), but different-site recurrences were more frequent in the surgically treated group (50% with surgery vs 31% with endovenous laser ablation, p=0.002). Overall, there was no significant difference in recurrence rates between groups. There were also no significant differences between groups in disease severity or QOL at five years.

Christenson et al (2010) compared endovenous laser ablation with ligation and stripping in 200 limbs (100 in each group). At 1-year follow-up, 98% of the limbs were reported to be free of symptoms. At two-year follow-up, the endovenous laser ablation group had two veins completely reopened and five 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. At one-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 five years, health-related QOL and CEAP classification improved in all groups with no significant differences among them. Grade I neovascularization was higher in the conventional surgery group (27% vs 3%, p<0.001), while grade II neovascularization did not differ significantly between surgical (17%) and endovenous laser ablation (13%) groups.

Wallace et al (2018) published the five-year outcomes of an RCT consisting of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins comparing surgery and endovenous laser ablation (EVLA) as treatments for symptomatic great saphenous varicose veins. Data from 218 patients were available at 5-year follow-up. The clinical recurrence rate was 34.4% for the surgery group and 20.9% for EVLA (p=0.010). Patients' QOL, 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=0.002; AVVQ: 13.69 to 4.59, p<0.001) and...
EVLA (EQ-5D: 0.808 to 1.0, p=0.002; AVVQ: 12.73 to 3.35, p<0.001). Technical success assessed by duplex ultrasound examination was 85.4% for surgery and 93.2% for EVLA (p=0.074).

### Table 1. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active Comparator</td>
</tr>
<tr>
<td>Brittenden (2014)&lt;sup&gt;10&lt;/sup&gt;</td>
<td>UK</td>
<td>11</td>
<td>2008-2012</td>
<td>Individuals with primary varicose veins</td>
<td>Foam sclerotherapy (n=286) or EVLA (n=210); Surgical treatment (n=289)</td>
</tr>
<tr>
<td>Rass (2012); RELACS</td>
<td>US</td>
<td>2</td>
<td>2004-2007</td>
<td>Individuals with GSV insufficiency</td>
<td>EVLA (n=185); Surgical treatment (n=161)</td>
</tr>
<tr>
<td>Wallace (2018)&lt;sup&gt;15&lt;/sup&gt;</td>
<td>UK</td>
<td>1</td>
<td>2004-2009 &lt;sup&gt;1&lt;/sup&gt;</td>
<td>Individuals with GSV insufficiency</td>
<td>EVLA (n=108); Surgical treatment (n=110)</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial; GSV: great saphenous vein; EVLA: endovenous laser ablation.

<sup>1</sup> Date of original intervention study

### Table 2. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>AVVQ Score at Baseline; 6 Months</th>
<th>Frequency of Procedural Complications</th>
<th>Rate of Same-Site Recurrence</th>
<th>Clinically Recurrent Varicose Veins</th>
<th>AVVQ Score at Baseline; 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brittenden (2014)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foam</td>
<td>17.69.9; 9.17.9</td>
<td></td>
<td>6%</td>
<td></td>
<td></td>
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<tr>
<td>Laser</td>
<td>17.89.1; 7.98.4</td>
<td></td>
<td>1%</td>
<td></td>
<td></td>
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<tr>
<td>Surgery</td>
<td>18.29.1; 7.87.5</td>
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<td>7%</td>
<td></td>
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<tr>
<td>P-value</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rass (2012); RELACS</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laser</td>
<td>18%</td>
<td></td>
<td>16.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>5%</td>
<td></td>
<td>23.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.002</td>
<td></td>
<td>0.15</td>
<td></td>
<td></td>
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<tr>
<td>Wallace (2018)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laser</td>
<td>20.9%</td>
<td></td>
<td>13.69; 4.59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>34.3%</td>
<td></td>
<td>12.73; 3.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.010</td>
<td></td>
<td>&lt;0.001</td>
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</tr>
</tbody>
</table>

AVVQ: Aberdeen Varicose Veins Questionnaire; RCT: randomized controlled trial.
Table 3. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population²</th>
<th>Intervention²</th>
<th>Comparator²</th>
<th>Outcomes²</th>
<th>Follow-Up²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brittenden (2014)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Longer follow-up needed</td>
</tr>
<tr>
<td>RELACS (2012)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wallace (2018)</td>
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</tbody>
</table>

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

² 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.

² Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

² Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

² 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.

² Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

The literature on the isolated treatment of the anterior accessory saphenous vein is limited. In a study by Theivacumar et al (2009), outcomes from a cohort of 33 patients who underwent endovenous laser ablation of the anterior accessory saphenous vein were compared with 33 matched controls undergoing endovenous laser ablation of the great saphenous vein. For 21 (64%) of the patients in the accessory saphenous vein group, there had been no previous treatment of the great saphenous vein. At 12-month follow-up, there was no evidence of reflux in these patients, and the treated accessory saphenous vein was not visible with ultrasound. AVVQ scores had improved in both groups, with no significant difference between them. Patient satisfaction scores were also similar.

Section 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**

**Physician-Compounded Sclerotherapy**

Hamann et al (2017) conducted a meta-analysis of RCTs reporting 5-year follow-up. 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<0.001).

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). 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. Thirty-two percent of legs treated initially with sclerotherapy required one 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 (GSV) insufficiency. Between 2008 and 2010, 166 individuals were randomized to receive open surgery, EVLA, or ultrasound-guided foam sclerotherapy. The GSV occlusion rate was 96% (95% CI: 91-100%) for open surgery, 89% (95% CI: 82-98%) for EVLA, and 51% (95% CI: 38-64%) for ultrasound-guided foam sclerotherapy (p<0.001). For patients with no additional treatment during follow-up, occlusion rates for open surgery, EVLA, and ultrasound-guided foam sclerotherapy were 96%, 89%, and 41%, respectively. The study was limited by the lack of blinding and by non-standardized foam application.

A noninferiority trial by Shadid et al (2012) compared foam sclerotherapy with ligation and stripping in 430 patients. 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 one week of treatment. Lam et al (2018) reported 8-year follow-up with 53% of the patients in the original trial. All measures of treatment success (eg, symptomatic GSV reflux, saphenofemoral junction failure, and recurrent reflux in the GSV) were lower in the physician-compounded sclerotherapy group compared to the ligation and stripping group.
Microfoam Sclerotherapy
In 2013, polidocanol (Varithena) microfoam was approved under a new drug application for the treatment of varicose veins. Efficacy data derived from two randomized, blinded, multicenter studies. 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 eight, as measured by the Varicose Vein Symptoms Questionnaire. The improvement in symptoms was greater in the pooled polidocanol treatment group (p<0.001) and in each of the individual dose-concentration groups compared with vehicle alone. Secondary and tertiary endpoints (appearance, duplex ultrasound response, QOL) were also significantly better for the polidocanol groups compared with controls. This second study, called to evaluate the efficacy and safety of polidocanal endovenous microfoam 0.5% and 1.0% compared to placebo for the treatment of saphenofemoral junction incompetence (VANISH-2), was published by Todd et al (2014). 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 five years is continuing.

Vasquez et al (2017) reported on a double-blinded RCT that evaluated the addition of polidocanol microfoam to endovenous thermal ablation. 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=0.001), 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=0.001) and patient (67% vs 50%, p=0.034) 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=0.037).

Section Summary: Sclerotherapy
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 two 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 Trials

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. Maximum visual analog scale 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=0.003). Average visual analog scale 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=0.003). Occlusion rates, clinical severity scores, disease-specific QOL, and generic QOL scores were similar between groups at one and six 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 (see Table 6).

Vahaaho et al (2019) reported a RCT that compared MOCA with endovenous thermal ablation (EVLA or RFA). 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 EVLA and RFA groups (p=0.002). Another randomized trial (Lam et al [2016]) reported interim results of a dose-finding study, finding greater closure with use of polidocanol 2% or 3% (liquid) than with polidocanol 1% (microfoam). Therefore, it is uncertain whether the concentration of sclerosant in the study by Vahaaho et al (2019) was optimal (see Table 5).

Table 5. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bootun et al (2016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lane et al (2017)</td>
<td>4. Strict inclusion criteria that may not be representative of intended use.</td>
<td>3. The concentration of sclerosant (1.5%) may not have been optimal.</td>
<td></td>
<td>1. Primary outcome was pain during the procedure</td>
<td>1. Outcomes only out to 6 mo</td>
</tr>
<tr>
<td>Vahaaho et al (2019)</td>
<td>4. Strict inclusion criteria that may not be representative of intended use.</td>
<td>3. The concentration of sclerosant (1.5%) may not have been optimal.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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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.

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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

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Follow-Up</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bootun et al (2016)²⁶; Lane et al (2017)²⁷</td>
<td>1. Patients not blinded to treatment (assessors of duplex ultrasound were blinded)</td>
<td>1.76% follow-up at 1 mo and 71% follow-up at 6 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vahaaho et al (2019)²⁴</td>
<td>1, 2, 3. Patients, surgeons, and assessors were not blinded to treatment</td>
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</tbody>
</table>

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

- **Allocation key:** 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
- **Blinding key:** 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
- **Selective Reporting key:** 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
- **Follow-Up 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).
- **Power key:** 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
- **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. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Systematic Reviews

Systematic reviews have included both of the two trials described above and within-subject comparisons. Sun et al (2017) included the 2 trials described above and 11 reports from prospective observational within-subjects comparisons.²⁸ They found mechanochemical endovenous ablation to be effective in the short-term with minimal complications, but lack of outcomes standardization precluded comparison with other techniques. Potential sources of bias in studies assessed included patient self-selection and lack of blinding, combined with subjective patient-reported outcomes measures. Overall, the quality of evidence was rated as low- or very-low.

By comparison, Witte et al (2017) evaluated 13 studies with 10 cohorts (1521 veins) using the MINORS study rating score.²⁹ The trials by Bootun et al (2016) and Lane et al (2017) as well as Lam et al (2016; described above) were rated as good quality. All studies were considered to have appropriate endpoints, unbiased assessment, and appropriate follow-up periods. Limitations of some studies included nonconsecutive enrollment, retrospective designs, and losses to follow-up of greater than 5%. None of the studies was designed to compare success with endothermal ablation. In the available cohort studies, short-term anatomic success ranged from 87% to 92% for the veins, with success rates of 91% (n=136; 95% CI, 85% to 95%) at 2 years and 87% (n=48; 95% CI, 75% to 94%) at three years. The longest follow-up study reported anatomic success (closure rates) of 87% at 3 years but with slightly lower clinical success (83%).³⁰

### Section Summary: MOCA

MOCA is a combination of liquid sclerotherapy and MOCA. The evidence on MOCA includes an RCT that compared MOCA to thermal ablation with one year results, an RCT with short-term results that compared MOCA with RFA, and case series with follow-up out to three years. The short-term results of one RCT suggested that intraprocedural pain is slightly lower with MOCA than with RFA. However, the second RCT showed lower occlusion rates than thermal ablation.
MOCA has been assessed in relatively few patients and for short durations. Longer follow-up in RCTs with a larger number of patients is needed to evaluate the efficacy and durability of this procedure compared with established procedures.

**Treatment of Saphenous Veins: Cyanoacrylate Adhesive**

The VenaSeal pivotal study (VeClose), a multicenter noninferiority trial with 222 patients, compared VenaSeal with RFA for the treatment of venous reflux.\(^{31,32}\) The pivotal registration study for the VeClose study and follow-up through 36 months have been published.\(^{31,32,33,34}\) These reports are summarized in Tables 7 and 8. The primary endpoint (the proportion of patients with complete closure of the target GSV 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, \(p=0.11\)). 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 (\(p<0.01\)). 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.\(^{35}\)

For the CAC and RFA groups, the complete occlusion rates were 97.2% and 97.0%. Freedom from recanalization was also similar between the two groups (\(p=0.08\)).\(^{33}\) Twenty-four month results were reported by Gibson et al (2018), which included 171 patients (87 from CAC and 84 from RFA).\(^{36}\) 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).\(^{34}\) Loss to follow-up was similar in the two groups. The complete closure rates for CAC and RFA were 94.4% and 91.9% (\(p=0.005\) 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 EVLA by Eroglu and Yasim (2018) in an RCT with 525 patients (see Table 7).\(^{37}\) Periprocedural outcomes showed a shorter intervention time, less pain, and shorter return to work with CAC compared to endovenous thermal ablation (see Table 8). There was no significant difference in occlusion rates between the three treatments at 6, 12, and 24 month follow-up.
### Table 7. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active</td>
</tr>
<tr>
<td>Eroglu and Yasim (2018)³⁷,</td>
<td>Asia</td>
<td>1</td>
<td>NR</td>
<td>525 patients ≥ 18 years with incompetence of the GSV (&gt;5.5 mm in diameter) or SSV (&gt;4 mm in diameter) and reflux &gt;0.5 sec.</td>
<td>175 VariClose CAC</td>
</tr>
</tbody>
</table>

CAC: cyanoacrylate ; CEAP: Clinical Etiology Anatomy Pathophysiology; EVLA: endovenous laser ablation; FDA: Food and Drug Administration; GSV: great saphenous vein; NR: not reported; RCT: randomized controlled trial; RFA: radiofrequency ablation; SSV: small saphenous vein; 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 8. Periprocedural Outcomes

<table>
<thead>
<tr>
<th>Eroglu and Yasim (2018)³⁷</th>
<th>Duration of Procedure min (sd)</th>
<th>Average Periprocedural Pain¹</th>
<th>2 or More Analgesics Used Daily n (%)</th>
<th>1 Day to Return to Work n (%)</th>
<th>2 Days to Return to Work n (%)</th>
<th>3 or More Days to Return to Work n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>503</td>
<td>503</td>
<td>456</td>
<td>456</td>
<td>456</td>
<td>456</td>
</tr>
<tr>
<td>VariClose</td>
<td>15.3 (2.6)</td>
<td>1 (mild)</td>
<td>105 (62.5)</td>
<td>161 (95.8)</td>
<td>7 (4.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>RFA</td>
<td>27.3 (7.7)</td>
<td>2 (moderate)</td>
<td>98 (65.8)</td>
<td>75 (50.3)</td>
<td>53 (35.6)</td>
<td>21 (14.1)</td>
</tr>
<tr>
<td>EVLA</td>
<td>35.0 (5.2)</td>
<td>2 (moderate)</td>
<td>105 (75.5)</td>
<td>105 (75.5)</td>
<td>24 (17.3)</td>
<td>10 (7.2)</td>
</tr>
<tr>
<td>p-Value</td>
<td>&lt;0.001</td>
<td>0.147²</td>
<td>&lt;0.001²</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Scale of 1 to 4; ²overall p-Value

EVLA: endovenous laser ablation; RFA: radiofrequency ablation.
### Table 9. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Vein Closure 1 month n (%)</th>
<th>Vein Closure 12 months n (%)</th>
<th>Vein Closure 24 months n (%)</th>
<th>Vein Closure 36 months n (%) or VCSS</th>
<th>Device Related Event n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>222</td>
<td>189</td>
<td>171</td>
<td>146</td>
<td>222</td>
</tr>
<tr>
<td>VenaSeal</td>
<td>107 (99.1%)(^2)</td>
<td>92 (96.7%)</td>
<td>82/86 (95.3%)</td>
<td>68/72 (94.4%)</td>
<td>31 (27%)</td>
</tr>
<tr>
<td>RFA</td>
<td>109 (95.6%)(^2)</td>
<td>91 (96.8%)</td>
<td>79/84 (94.0%)</td>
<td>68/74 (91.9%)</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>Eroglu and Yasim (2018)(^{37})</td>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
<td>VCSS at 24 months</td>
</tr>
<tr>
<td>N</td>
<td>503</td>
<td>456</td>
<td>456</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VariClose</td>
<td>98.1%</td>
<td>94.1%</td>
<td>95.1%</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>RFA</td>
<td>94.7%</td>
<td>92.5%</td>
<td>94.2%</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>EVLA</td>
<td>92.6%</td>
<td>90.9%</td>
<td>91.5%</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>p-Value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

EVL: endovenous laser ablation; 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 10 and 11. The primary limitation of the pivotal study of VenaSeal is the loss to follow-up at two and three years, with equal loss to follow-up was similar in the two groups. The study by Eroglu and Yasim (2018) had 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 10. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population a</th>
<th>Intervention b</th>
<th>Comparator c</th>
<th>Outcomes d</th>
<th>Follow-Up e</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morrison (2015), 32, Morrison (2017), 33, Gibson (2018)(^{36}), VeClose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Follow-up scheduled to continue to 3 years</td>
</tr>
<tr>
<td>Morrison (2018)(^{34})</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1. Follow-up will continue to 60 months</td>
</tr>
<tr>
<td>Eroglu and Yasim (2018)(^{37})</td>
<td>2. This specific cyanoacrylate product is not currently available in the US</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.
Table 11 Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Follow-Up</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morrison (2015), 32</td>
<td>1, 2, 3</td>
<td></td>
<td></td>
<td>1. &gt;20% loss to follow-up</td>
<td></td>
<td>3. variable reporting of CI and p values</td>
</tr>
<tr>
<td>Morrison (2017), 33</td>
<td></td>
<td>1, 3. The outcome was assessed by the treating physician and patients were not blinded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gibbons (2018) 36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morrison et al (2018) 34 VeClose</td>
<td>1, 2, 3. Patients were notified of the group assignment a day before the procedure</td>
<td></td>
<td></td>
<td>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</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eroglu and Yasim (2018) 37</td>
<td></td>
<td>1, 2, 3. Patients were notified of the group assignment a day before the procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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


d Follow-Up 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. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Eroglu et al (2017) reported closure rates of 94.1% at 30 months in a prospective cohort of 159 patients.38 Thirty-three-month follow-up was reported by Zierau (2015) for 467 (58.7%) of 795 veins treated at 1 institution in Germany.39 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 month follow-up. The short-term efficacy of VenaSeal CAC has been shown to be noninferior to RFA at up to 36-month 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 two groups at the long-term follow-up and is not expected to influence the 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-month 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**

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. Forty-four percent of patients had residual GSV 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. Included were 120 patients with symptomatic uncomplicated varicose veins (CEAP class C2) with saphenofemoral incompetence and GSV 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 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=NS). 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=NS). 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 two or five-month follow-ups for endovenous laser ablation.

**Section 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 question addressed in this evidence review is: Does the use of ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins improve the net health outcome in individuals who have varicose tributary veins?

The following PICOTS were used to select literature to inform this review.
**Patients**
The relevant population of interest are individuals who have varicose tributary veins.

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

**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 QOL. 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 principles outlined for indications one through five.

**Sclerotherapy and Phlebectomy**
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 by Tisi et al (2006), based primarily on RCTs from the 1980s, concluded that: "The evidence supports the current place of sclerotherapy in modern clinical practice, which is usually limited to treatment of recurrent varicose veins following surgery and thread veins."43, Sclerotherapy and phlebectomy are considered appropriate in the absence of reflux of the saphenous system (eg, post- or adjunctive treatment to other procedures such as surgery)40. 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.41, QOL 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 GSV with visual foam sclerotherapy for varicose tributary veins.44, 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=NS). 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. 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 clinicians' 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**

A meta-analysis by Luebke and Brunkwall (2008) included 5 studies that compared TIPP with conventional surgery. 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. Included in the meta-analysis was an RCT by Chetter et al (2006) that compared TIPP (n=29) with a multiple stab incision procedure (n=33). A single surgeon performed all but two 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 one and six weeks postsurgery. 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 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 QOL.

**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**

The purpose of ablation (eg, subfascial endoscopic perforator surgery) of perforator veins in patients who have perforator vein reflux is to provide a treatment option that is an alternative to or an improvement on existing therapies.
The question addressed in this evidence review is: Does the use of ablation (eg, subfascial endoscopic perforator surgery) of perforator veins improve the net health outcome in individuals who have perforator vein reflux?

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

**Patients**
The relevant population of interest are individuals who have perforator vein reflux.

**Interventions**
The therapy being considered is ablation (eg, subfascial endoscopic perforator surgery) of perforator veins.

**Comparators**
The following therapy is currently being used to treat perforator vein reflux: conservative therapy.

**Outcomes**
The general outcomes of interest are reductions in symptoms and morbid events, change in disease status, and improvements in QOL.

Follow-up at two years is of interest for ablation (eg, subfascial endoscopic perforator surgery) of perforator veins to monitor relevant outcomes.

**Study Selection Criteria**
Methodologically credible studies were selected using the principles outlined for indications one through five.

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-C6). The four trials included two level I (large subject population) and two 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 two treated the GSV alone. The 2 randomized studies (2004, 2007) in which the GSV alone was treated (including the ESCHAR trial) showed a significant reduction in ulcer recurrence compared with conservative therapy.48,49 A community hospital–based multicenter, double-blind, randomized trial reported by Nelzen and Fransson (2011) found no clinical benefit (self-reported symptoms) from adding subfascial endoscopic perforator surgery to saphenous surgery in 75 patients with varicose ulcers (CEAP classes C5-C6) and incompetent perforators.50,51

Treatment of the GSV 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.51 O'Donnell (2008) discussed additional (lower quality) evidence to suggest deep venous valvular involvement rather than incompetent perforators in venous insufficiency. 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
Tenbrook et al (2004) reviewed the literature on subfascial endoscopic perforator surgery, which
included 19 case series and 1 randomized trial. In total, the selected studies included 1031
patients with 1140 treated limbs. Reviewers concluded that subfascial endoscopic perforator
surgery was associated with excellent results regarding ulcer healing and prevention of
recurrence. However, they also noted that randomized trials are required to define the relative
contributions of compression therapy, superficial venous surgery, and subfascial endoscopic
on 10-year follow-up from a randomized trial that compared conservative treatment with
subfascial endoscopic perforator surgery for venous leg ulcers. Patients (196 legs) returned to
the clinic annually, and analysis was conducted with the last-observation carried forward. The
primary outcome (incidence ulcer-free) was significantly higher in the surgical group (58.9%)
than in the conservative treatment group (39.6%; p=0.007). The number of incompetent
perforator veins at follow-up was a risk factor for not being ulcer-free (OR=18.5, p<0.001). The
relatively high rate of recurrence in the surgically treated group might have been due to limited
or no stripping of the superficial veins at the time of subfascial endoscopic perforator surgery.

In a meta-analysis of subfascial endoscopic perforator surgery 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."54
Reviewers also stated that the "introduction of less invasive techniques for perforator vein
ablation, such as ultrasound-guided sclerotherapy or radiofrequency ablation, may diminish the
role of subfascial endoscopic perforator surgery in the future."

Other Treatments
In a review of procedures for management of varicose veins, Hirsch and Dillavou (2008)
recommended duplex-guided foam sclerotherapy, microincision phlebectomy, or thermal ablation
using a short RFA catheter for the treatment of symptomatic residual perforator vein
incompetence. Ablation of incompetent perforator veins with laser or RFA has been shown to
be technically feasible, although no studies have been identified that showed improvements in
clinical outcomes (eg, ulcer healing or recurrence). A literature update by Hissink et al (2010)
identified 1 study of endovenous laser ablation for perforating veins assessing 33 patients with
CEAP classifications of C4 (skin changes), C5 (healed ulcer), or C6 (active ulcer). All
incompetent saphenous trunks were treated simultaneously (63% of limbs). At 3-month follow-
up, occlusion was achieved in 78% of the perforating veins. Five (15%) patients had active ulcers
at baseline; 4 of the 5 ulcers had healed by 6 weeks after endovenous laser ablation. Evidence
on the treatment of perforator veins with ultrasound-guided sclerotherapy is limited, and there is
a risk of deep venous occlusion.

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 (ie, ulcers), treatment of perforator vein reflux may be as beneficial as any alternative (eg, deep vein valve replacement). Comparative studies are needed to determine the most effective method of ligating and ablating incompetent perforator veins. Subfascial endoscopic perforator surgery has been shown to be as effective as the Linton procedure with a reduction in adverse events. Although only one case series has been identified showing an improvement in health outcomes, 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.

**Summary of Evidence**

**Saphenous Veins**

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive endovenous thermal ablation (radiofrequency or laser), the evidence includes RCTs and systematic reviews of controlled trials. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. There are a number of large RCTs and systematic reviews of RCTs assessing endovenous thermal ablation of the saphenous veins. Comparison with the standard of ligation and stripping at 2- to 5-year follow-up has supported the use of both endovenous laser ablation and RFA. Evidence has suggested that ligation and stripping lead to more neovascularization, while thermal ablation leads to more recanalization, resulting in similar clinical outcomes for endovenous thermal ablation and surgery. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive microfoam sclerotherapy, the evidence includes RCTs. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. For physician-compounded sclerotherapy, there is high variability in success rates and some reports of serious adverse events. By comparison, rates of occlusion with the microfoam sclerotherapy (polidocanol 1%) approved by the FDA are similar to those reported for endovenous laser ablation or stripping. Results of a noninferiority trial of physician-compounded sclerotherapy have indicated that once occluded, recurrence rates at two years are similar to those of ligation and stripping. Together, this evidence indicates that the more consistent occlusion with the microfoam sclerotherapy preparation will lead to recurrence rates similar to ligation and stripping in the longer term. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Based on the available evidence, clinical input obtained in 2015, and clinical practice guidelines, the use of endovenous RFA, endovenous laser ablation, and microfoam sclerotherapy are considered to improve outcomes when used in the saphenous veins. For treatment of saphenous tributaries at the same time or following treatment of the saphenous vein, stab avulsion, hook phlebectomy, sclerotherapy, or transilluminated powered phlebectomy improve outcomes.

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive MOCA, the evidence includes two RCTs and case series. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. MOCA is a combination of liquid sclerotherapy with mechanical abrasion. Potential advantages of this procedure compared with thermal ablation are that MOCA does not require multiple needle sticks with tumescent anesthesia and may result in less pain during the procedure. The evidence on MOCA includes an RCT that compared MOCA to thermal ablation with one year results, an RCT with short-term...
results that compared MOCA with RFA, and case series with follow-up out to three years. The short-term results of one RCT suggested that intraprocedural pain is slightly lower with MOCA than with RFA. However, the second RCT showed lower occlusion rates than thermal ablation. MOCA has been assessed in relatively few patients and for short durations. Longer follow-up in RCTs with a larger number of patients is needed to evaluate the efficacy and durability of this procedure compared with established procedures. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive CAC, the evidence includes two RCTs and a prospective cohort. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. Evidence 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-month follow-up. The short-term efficacy of VenaSeal CAC has been shown to be noninferior to RFA at up to 36 months. 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 the 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-month follow-up. The CAC procedure and return to work were shorter and pain scores were lower compared to thermal ablation, although 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. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive cryoablation, the evidence includes RCTs and multicenter series. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. Results from a recent RCT of cryoablation have indicated that this therapy is inferior to conventional stripping. Studies showing a benefit on health outcomes are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Varicose Tributary Veins**

For individuals who have varicose tributary veins who receive ablation (stab avulsion, sclerotherapy, or phlebectomy) of tributary veins, the evidence includes RCTs and systematic reviews of RCTs. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. The literature has shown that sclerotherapy is effective for treating 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 to available alternatives such as stab avulsion and hook phlebectomy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Perforator Veins**

For individuals who have perforator vein reflux who receive ablation (eg, subfascial endoscopic perforator surgery) of perforator veins, the evidence includes RCTs and systematic reviews of
RCTs. The relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. The literature has indicated that the routine ligation or ablation of incompetent perforator veins is not necessary for the treatment of varicose veins/venous insufficiency at the time of 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 an alternative (e.g., deep vein valve replacement). Comparative studies are needed to determine the most effective method of ligating or ablating incompetent perforator veins. Subfascial endoscopic perforator surgery has been shown to be as effective as the Linton procedure with a reduction in adverse events. Although only one case series has been identified showing an improvement in health outcomes, endovenous ablation with specialized laser or radiofrequency probes has been shown to effectively ablate incompetent perforator veins with a potential decrease in morbidity compared with surgical interventions. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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
Society for Vascular Surgery and American Venous Forum

Table 12. Guidelines on Management of Varicose Veins and Associated Chronic Venous Diseases

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>SOR</th>
<th>QOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compression therapy for venous ulcerations and varicose veins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compression therapy is recommended as the primary treatment to aid healing of venous ulceration</td>
<td>1B</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>To decrease the recurrence of venous ulcers, ablation of the incompetent superficial veins in addition to compression therapy is recommended</td>
<td>1A</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Use of compression therapy for patients with symptomatic varicose veins is recommended</td>
<td>2C</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Compression therapy as the primary treatment if the patient is a candidate for saphenous vein ablation is not recommended</td>
<td>1B</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Treatment of the incompetent great saphenous vein</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td>1B</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Contains Public Information
### Recommendation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>SOR</th>
<th>QOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicose tributaries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phlebectomy or sclerotherapy are recommended to treat varicose tributaries</td>
<td>1B</td>
<td>Strong Moderate</td>
<td></td>
</tr>
<tr>
<td>Transilluminated powered phlebectomy using lower oscillation speeds and extended tumescence is an alternative to traditional phlebectomy</td>
<td>2C</td>
<td>Weak Low</td>
<td></td>
</tr>
<tr>
<td>Perforating vein incompetence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective treatment of perforating vein incompetence in patients with simple varicose veins is not recommended</td>
<td>1B</td>
<td>Strong Moderate</td>
<td></td>
</tr>
<tr>
<td>Treatment of pathologic perforating veins (outward flow of $\geq$500 ms duration, with a diameter of $\geq$3.5 mm) located underneath healed or active ulcers (CEAP class C5-C6) is recommended</td>
<td>2B</td>
<td>Weak Moderate</td>
<td></td>
</tr>
</tbody>
</table>

QOE: quality of evidence; SOR: strength of recommendation.

* 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.

### Society of Interventional Radiography

The Society of Interventional Radiography (2003) published a position statement that considered endovenous ablation therapy, using either laser or radiofrequency devices under imaging guidance and monitoring, an effective treatment of extremity venous reflux and varicose veins under the following conditions:

"The endovenous treatment of varicose veins may be medically necessary when:

1. one of the following indications (A - E) is present:
   
   A. Persistent symptoms interfering with activities of daily living in spite of conservative/nonsurgical management. Symptoms include aching, cramping, burning, itching, and/or swelling during activity or after prolonged standing.
   
   B. Significant recurrent attacks of superficial phlebitis
   
   C. Hemorrhage from a ruptured varix
   
   D. Ulceration from venous stasis where incompetent varices are a contributing factor
   
   E. Symptomatic incompetence of the great or small saphenous veins (symptoms as in A above) and;

2. A trial of conservative, nonoperative treatment has failed. This would include mild exercise, avoidance of prolonged immobility, periodic elevation of legs, and compressive stockings.

3. The patient's anatomy is amenable to endovenous ablation."

In a joint statement, American Venous Forum and Society of Interventional Radiography (2007) recommended reporting standards for endovenous ablation for the treatment of venous insufficiency. They recommended that reporting in clinical studies should include the symptoms of venous disease, history of the disease and prior treatment, the presence of major comorbidities, and any exclusion criteria. It was noted that potential candidates for endovenous ablation might include patients with reflux in an incompetent great saphenous vein or smaller saphenous vein or a major tributary branch of the great or smaller saphenous veins such as the anterior thigh circumflex vein, posterior thigh circumflex vein, or anterior accessory great saphenous vein. The presence of reflux in these veins is important to document using duplex ultrasound imaging, and the ultrasound criteria used to define reflux should be indicated. It was also stated that, in current practice, most vascular laboratories consider the presence of venous flow reversal for greater than 0.5 to 1.0 second with proximal compression, Valsalva maneuver, or distal compression and release to represent pathologic reflux.
American College of Phlebology
The American College of Phlebology (2017) published guidelines on the treatment of refluxing accessory saphenous veins.\textsuperscript{37} 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
The NICE (2013) updated its guidance on ultrasound-guided foam sclerotherapy for varicose veins.\textsuperscript{24} 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."

The NICE (2016) 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..."\textsuperscript{61}.

The NICE (2013) published guidance on the diagnosis and management of varicose veins in the leg.\textsuperscript{62} The NICE (2015) published a technology assessment on the clinical effectiveness and cost-effectiveness of foam sclerotherapy, endovenous laser ablation, and surgery for varicose veins.\textsuperscript{63} Five-year trial results are currently being evaluated.

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

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 13.

Table 13. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
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<td></td>
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<tr>
<td>NCT03392753</td>
<td>Randomised Controlled Trial of Mechanochemical Ablation Versus Cyanacrylate Adhesive for the Treatment of Varicose Veins</td>
<td>180</td>
<td>Dec 2020</td>
</tr>
<tr>
<td>NTR4613\textsuperscript{a}</td>
<td>Mechanoechemical endovenous ablation versus radiofrequency ablation in the treatment of primary small saphenous vein insufficiency (MESSI trial)</td>
<td>160</td>
<td>Apr 2020</td>
</tr>
<tr>
<td>NCT01936168</td>
<td>Mechanoechemical endovenous ablation versus radiofrequency ablation in the treatment of primary great saphenous vein incompetence (MARADONA)</td>
<td>460</td>
<td>Dec 2020</td>
</tr>
<tr>
<td>NCT No.</td>
<td>Trial Name</td>
<td>Planned Enrollment</td>
<td>Completion Date</td>
</tr>
<tr>
<td>-----------</td>
<td>----------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>NCT02627846</td>
<td>A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency (LAMA)</td>
<td>140</td>
<td>Sep 2030</td>
</tr>
</tbody>
</table>

NCT: national clinical trial. NTR: Netherlands Trial Registry.

* Denotes industry-sponsored or cosponsored trial.

**CODING**

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

**CPT/HCPCS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36465</td>
<td>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 (eg, great saphenous vein, accessory saphenous vein)</td>
</tr>
<tr>
<td>36466</td>
<td>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 (eg, great saphenous vein, accessory saphenous vein), same leg</td>
</tr>
<tr>
<td>36468</td>
<td>Single or multiple injections of sclerosing solutions, spider veins (telangiectasia); limb or trunk</td>
</tr>
<tr>
<td>36470</td>
<td>Injection of sclerosing solution: single vein</td>
</tr>
<tr>
<td>36471</td>
<td>Injection of sclerosing solution; multiple veins, same leg</td>
</tr>
<tr>
<td>36473</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated</td>
</tr>
<tr>
<td>36474</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>36475</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated</td>
</tr>
<tr>
<td>36476</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; second and subsequent veins treated in a single extremity, each through separate access sites (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>36478</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated</td>
</tr>
<tr>
<td>36479</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; second and subsequent veins treated in a single extremity, each through separate access sites (list separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>
36482 Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (eg, 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 (eg, 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

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 leg, 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

76937 Ultrasound guidance for vascular access requiring ultrasound evaluation of potential access sites, documentation of selected vessel patency, concurrent realtime ultrasound visualization of vascular needle entry, with permanent recording and reporting (List separately in addition to code for primary procedure)

76942 Ultrasonic guidance for needle placement (e.g., biopsy, aspiration, injection, localization device), imaging supervision and interpretation

76998 Ultrasonic guidance, intraoperative

76999 Unlisted ultrasound procedure (e.g. diagnostic, interventional)

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

0524T Endovenous catheter directed chemical ablation with balloon isolation of incompetent extremity vein, open or percutaneous, including all vascular access, catheter manipulation, diagnostic imaging, imaging guidance and monitoring (Effective 01-01-2019)

S2202 Echosclerotherapy

- Note: The bulk of the literature discussing the role of ultrasound guidance refers to sclerotherapy of the saphenous vein, as opposed to the varicose tributaries. If ultrasound
guidance (CPT code 76942) is used to guide sclerotherapy of the varicose tributaries, it would be considered content of service to the injection procedure.

ICD-10 Diagnoses (Effective October 1, 2015)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>I83.011</td>
<td>Varicose veins of right lower extremity with ulcer of thigh</td>
</tr>
<tr>
<td>I83.012</td>
<td>Varicose veins of right lower extremity with ulcer of calf</td>
</tr>
<tr>
<td>I83.013</td>
<td>Varicose veins of right lower extremity with ulcer of ankle</td>
</tr>
<tr>
<td>I83.014</td>
<td>Varicose veins of right lower extremity with ulcer of heel and midfoot</td>
</tr>
<tr>
<td>I83.015</td>
<td>Varicose veins of right lower extremity with ulcer other part of foot</td>
</tr>
<tr>
<td>I83.018</td>
<td>Varicose veins of right lower extremity with ulcer other part of lower leg</td>
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<td>I83.021</td>
<td>Varicose veins of left lower extremity with ulcer of thigh</td>
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<tr>
<td>I83.022</td>
<td>Varicose veins of left lower extremity with ulcer of calf</td>
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<tr>
<td>I83.023</td>
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<td>I83.024</td>
<td>Varicose veins of left lower extremity with ulcer of heel and midfoot</td>
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<tr>
<td>I83.025</td>
<td>Varicose veins of left lower extremity with ulcer other part of foot</td>
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<tr>
<td>I83.028</td>
<td>Varicose veins of left lower extremity with ulcer other part of lower leg</td>
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<td>I83.11</td>
<td>Varicose veins of right lower extremity with inflammation</td>
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<td>I83.12</td>
<td>Varicose veins of left lower extremity with inflammation</td>
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<tr>
<td>I83.211</td>
<td>Varicose veins of right lower extremity with both ulcer of thigh and inflammation</td>
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<tr>
<td>I83.212</td>
<td>Varicose veins of right lower extremity with both ulcer of calf and inflammation</td>
</tr>
<tr>
<td>I83.213</td>
<td>Varicose veins of right lower extremity with both ulcer of ankle and inflammation</td>
</tr>
<tr>
<td>I83.214</td>
<td>Varicose veins of right lower extremity with both ulcer of heel and midfoot and inflammation</td>
</tr>
<tr>
<td>I83.215</td>
<td>Varicose veins of right lower extremity with both ulcer other part of foot and inflammation</td>
</tr>
<tr>
<td>I83.218</td>
<td>Varicose veins of right lower extremity with both ulcer of other part of lower extremity and inflammation</td>
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<td>I83.219</td>
<td>Varicose veins of right lower extremity with both ulcer of unspecified site and inflammation</td>
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<td>Varicose veins of left lower extremity with both ulcer of thigh and inflammation</td>
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<td>I83.222</td>
<td>Varicose veins of left lower extremity with both ulcer of calf and inflammation</td>
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<td>I83.223</td>
<td>Varicose veins of left lower extremity with both ulcer of ankle and inflammation</td>
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<tr>
<td>I83.228</td>
<td>Varicose veins of left lower extremity with both ulcer of other part of lower extremity and inflammation</td>
</tr>
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<td>I83.811</td>
<td>Varicose veins of right lower extremities with pain</td>
</tr>
<tr>
<td>I83.812</td>
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<td>I83.813</td>
<td>Varicose veins of bilateral lower extremities with pain</td>
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<tr>
<td>I83.891</td>
<td>Varicose veins of right lower extremities with other complications</td>
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<td>I83.892</td>
<td>Varicose veins of left lower extremities with other complications</td>
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<td>I83.92</td>
<td>Asymptomatic varicose veins of left lower extremity</td>
</tr>
<tr>
<td>I83.93</td>
<td>Asymptomatic varicose veins of bilateral lower extremities</td>
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**REVISIONS**

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<td>Description section updated</td>
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<tr>
<td></td>
<td>In Policy section:</td>
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<tr>
<td></td>
<td>• Clarified policy by including within the Greater or Lesser Saphenous Veins, Accessory Saphenous Veins, and Symptomatic Varicose Tributaries sections of the policy the following:</td>
</tr>
<tr>
<td></td>
<td>&quot;B. Physical findings that support medically significant venous hypertension must be clearly documented.&quot; and</td>
</tr>
</tbody>
</table>
## REVISIONS

“D. Treatment of varicose veins for cosmetic purposes is not covered.”

- Clarified Policy Guidelines by:
  - Adding to #1: “Physical findings that support medically significant venous hypertension must be clearly documented. Treatment of varicose veins for cosmetic purposes is not covered.” to read “1. A clear and complete description of the physical exam of the lower extremities that documents the medical necessity of treatment for venous insufficiency for medical, not cosmetic purposes, is required. Physical findings that support medically significant venous hypertension must be clearly documented. Treatment of varicose veins for cosmetic purposes is not covered. Photographs may be requested.”
  - Revising #2: From “...up to 3 sclerotherapy sessions for both legs...” to “...up to 3 sclerotherapy sessions for each leg...” to read “Up to 20 injections in each leg may be treated in any one session and up to 3 sclerotherapy sessions for each leg may be considered medically necessary if selection criteria are met.”
  - Added to Policy Guidelines:
    - 5. Patients with combined deep and superficial venous insufficiency are often not good candidates for ablation therapy. Varicose vein recurrence and ulcer recurrence rates following intervention are much higher.”
  - Removed from Policy Guidelines:
    - “The severity of signs and symptoms of venous disease tends to correlate with the degree of reflux identified by duplex ultrasound.”
  - The intent of the policy language was not changed.

### Rationale section update

### Revision section:

- Removed revision details for 01-04-2008 and 07-18-2008

### References updated

### Description section updated.

In Policy section:

- Within the subsection of Greater or Lesser Saphenous Veins moved the following wording as a stand alone Item B. to be included with the medically necessary criteria as item A. 3. to read, “Physical findings that support medically significant venous hypertension are clearly documented.” This change was made to be clearer that in addition to meeting the medical necessity criteria, physical findings that support medically significant venous hypertension must be clearly documented.

- Within the subsection of Accessory Saphenous Veins moved the following wording as a stand alone Item B. to be included with the medically necessary criteria as item A. 4. to read, “Physical findings that support medically significant venous hypertension are clearly documented.” This change was made to be clearer that in addition to meeting the medical necessity criteria, physical findings that support medically significant venous hypertension must be clearly documented.

- Within the subsection of Symptomatic Varicose Tributaries, Item A. was liberalized from, “The following treatments are considered medically necessary as a component of the treatment of symptomatic varicose tributaries when performed either at the same time or following prior treatment (surgical, radiofrequency or laser) of the saphenous veins...” to “The following treatments are considered medically necessary as a component of the treatment of symptomatic varicose tributaries...”

- Within the subsection of Symptomatic Varicose Tributaries, Item B. was revised from “Physical findings that support medically significant venous hypertension must be clearly documented.” to “Physical findings must support medical necessity.”

### Rationale section updated

### References updated

### Description section updated

09-11-2012 Description section updated
**REVISIONS**

In Policy section:
- In I A 2 c and II A 3 c revised wording from "Recurrent hemorrhage or bleeding episodes..." to "Hemorrhage or recurrent bleeding episodes..." No policy intent change was made.
- In I A 3 and II A 4 clarified the wording from "Physical findings..." to "Physical / visible findings..."
- Added to IV Perforator Veins
  
  "A. Surgical ligation (including subfascial endoscopic perforator surgery) or endovenous radiofrequency or laser ablation of incompetent perforator veins may be considered medically necessary as a treatment of leg ulcers associated with chronic venous insufficiency when the following conditions have been met:
  1. There is demonstrated perforator reflux; AND
  2. The superficial saphenous veins (greater, lesser, or accessory saphenous and symptomatic varicose tributaries) have been previously eliminated; AND
  3. Ulcers have not resolved following combined superficial vein treatment and compression therapy for at least 3 months; AND
  4. The venous insufficiency is not secondary to deep venous thromboembolism."
- Moved from Policy Guidelines to IV B the not medically necessary indication of:
  
  "6. Perforator reflux often resolves following saphenous ablation."
- Added the not medically necessary indication of IV C: "C. Ligation or ablation of incompetent perforator veins performed concurrently with superficial venous surgery is not medically necessary."
- In Policy Guidelines #4 added, "However, deep vein insufficiency is not a contraindication to superficial vein treatment."
- In Policy Guidelines Reimbursement sub-section item 1 revised, "...reimbursed at 25% of full." to read, "1. Endovenous ablation (36475, 36476, 36478 and 36479) other than the greater saphenous vein will be reimbursed at 50% of full."

Rationale section updated

In Revision section:

References updated

03-08-2013
- In the Reimbursement section:
  
  "Removed the reimbursement limitation stating, "Endovenous ablation (36475, 36476, 36478 and 36479) other than the greater saphenous vein will be reimbursed at 50% of full.""

12-24-2014
- Description section updated

In Policy section:
- In Item I A and II A removed "Physical / visible findings that support medically significant venous hypertension are clearly documented." And added "...or microfoam sclerotherapy..." to read "...by surgery (ligation and stripping), endovenous radiofrequency or laser ablation, or microfoam sclerotherapy may be considered medically necessary for..."
- In Item I B added "...or microfoam sclerotherapy..." to read "...by surgery, endovenous radiofrequency or laser ablation, or microfoam sclerotherapy that do not meet the criteria described above is considered not medically necessary."
- In Item II A added "1. Incompetence of the accessory saphenous vein is isolated, OR"
- In Item II A added "...or microfoam sclerotherapy..." to read "...by surgery, endovenous radiofrequency or laser ablation, or microfoam sclerotherapy that do not meet the criteria described above is considered not medically necessary."
- In Item II A added "1. Incompetence of the accessory saphenous vein is isolated, OR" to read "Incompetence of the accessory saphenous vein is isolated, OR The greater or lesser saphenous veins had been previously eliminated (at least 3 months);"
- In Item III A added "When physical findings support medical necessity," (formerly standalone Item III B) to read, "When physical findings support medical necessity, the following treatments are considered medically necessary as a component of the treatment of symptomatic varicose tributaries (none of these techniques has been shown to be superior to another):"
### REVISIONS

- In new Item III B removed "Sclerotherapy as" to read, "The sole treatment of varicose vein tributaries..."
- In Policy Guidelines added "5. It should be noted that the bulk of the literature discussing the role of ultrasound guidance refers to sclerotherapy of the saphenous vein, as opposed to the varicose tributaries."
- In Policy Guidelines removed "There is little evidence to support that ultrasound guidance makes a significant difference in outcomes from sclerotherapy when compared to non-ultrasound guided techniques."

**Rationale section updated**

**In Coding section:**
- Removed CPT Code: 36469 (Effective January 1, 2015)
- Coding comments updated
- ICD-10 Codes added

**In Revision section**
- Removed Revision details for 10-11-2010.
- References updated

01-01-2016  In Coding section:
- Removed CPT codes: 37250, 37251


**Description section updated**

**In Policy section:**
- Throughout the policy removed "lesser" and added "small" to read "great or small saphenous veins"
- In Item I revised to read "SAPHENOUS VEINS – Great or Small Saphenous Veins"
- In Item I A 1 added "and CEAP [Clinical, Etiology, Anatomy, Pathophysiology], class C2 or greater" to read "There is demonstrated saphenous reflux and CEAP [Clinical, Etiology, Anatomy, Pathophysiology], class C2 or greater"
- In Item I A 2a and II A 3a removed "that fails to respond to compressive therapy" to read "Ulceration secondary to venous stasis"
- In Item I A 2b and II A 3b removed "that fails to respond to compressive therapy" to read "Recurrent superficial thrombophlebitis"
- In Item I A 2d1) removed "or significant refractory edema or refractory stasis dermatitis when" to read "Persistent pain, swelling, itching, burning, or other symptoms associated with saphenous reflux"
- In Item II A 3d1) removed "or significant refractory edema or refractory stasis dermatitis when" and "accessory vein" to read "Persistent pain, swelling, itching, burning, or other symptoms associated with saphenous reflux"
- In Item II B added "veins by surgery, endovenous radiofrequency or laser ablation, or microfoam sclerotherapy" to read "Treatment of accessory saphenous veins by surgery, endovenous radiofrequency or laser ablation, or microfoam sclerotherapy, that do not meet the criteria described above is considered not medically necessary."
- In Item III A removed "When physical findings support medical necessity" and added "when performed either at the same time or following prior treatment (surgical, radiofrequency or laser) of the saphenous veins" to read "The following treatments are considered medically necessary as a component of the treatment of symptomatic varicose tributaries when performed either at the same time or following prior treatment (surgical, radiofrequency or laser) of the saphenous veins (none of these techniques has been shown to be superior to another):"
- In Item III B removed "The sole", "in the presence of saphenofemoral or saphenopopliteal reflux" and not medically necessary" and added "symptomatic", "when performed either at the same time or following prior treatment of saphenous veins using any other techniques than noted above" and "experimental / investigational" to read
## REVISIONS

"Treatment of symptomatic varicose tributaries when performed either at the same time or following prior treatment of saphenous veins using any other techniques than noted above reflux is considered experimental / investigational"
- In Item VI added "Veins" to read "Other Veins"
- In Item VI A revised "not medically necessary" to "experimental / investigational" to read "Techniques for conditions not specifically listed above are experimental / investigational, including, but not limited to:"
  - In Item VI A added "techniques, other than microfoam sclerotherapy, of great, small, or accessory saphenous veins", "Sclerotherapy of perforator veins", "Mechanochemical ablation of any vein", "Cyanoacrylate adhesive of any vein" to read "1. Sclerotherapy techniques, other than microfoam sclerotherapy, of great, small, or accessory saphenous veins
2. Sclerotherapy of perforator veins
3. Sclerotherapy of isolated tributary veins without prior or concurrent treatment of saphenous veins
4. Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy of perforator, great or small saphenous, or accessory saphenous veins.
5. Endovenous radiofrequency or laser ablation of tributary veins
6. Mechanochemical ablation of any vein
7. Cyanoacrylate adhesive of any vein
8. Endovenous cryoablation of any vein"
- Policy Guidelines updated

### Rationale section updated

In Coding section:
- Added CPT Codes: 36465, 36466, 36473, 36474, 36482, 36483, 0524T
- Removed CPT Code: 93965

### References updated

09-13-2019

### Description section updated

In Policy section:
- In Items I A, I B, II A, II B, IV A revised the phrase "endovenous radiofrequency or laser ablation" to read "endovenous thermal ablation (radiofrequency or laser)"
- Added Item I C "Treatment of the great or small saphenous veins by cyanoacrylate adhesive is considered not medically necessary for symptomatic varicose veins / venous insufficiency (see Policy Guideline 1)."
- In Item II A 1 a added "when documentation of the anatomy supports the reflux" to read "Incompetence of the accessory saphenous vein, when documentation of the anatomy supports the reflux is isolated"
- Added Item C "Treatment of accessory saphenous veins by cyanoacrylate adhesive is considered not medically necessary for symptomatic varicose veins / venous insufficiency (see Policy Guideline 1)."
- In Item VI A removed from the E/I statement "cyanoacrylate adhesive of any vein"
- In Policy Guidelines added:
  "1. For a service to be considered medically necessary, it should not be more costly than an alternative service or supply or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results for the illness, injury, or disease."

### Rationale section updated

In Coding section:
- Updated coding notations.

### References updated
REFERENCES
19. Todd KL, 3rd, Wright D, for the Vanish-Investigator Group. The VANISH-2 study: a randomized, blinded, multicenter study to evaluate the efficacy and safety of polidocanol endovenous microfoam 0.5% and 1.0% compared with placebo for the treatment of saphenofemoral junction incompetence. Phlebology. Oct 2014;29(9):608-618. PMID 23864535

20. Eroglu, EE, Yasim, AA. A Randomised Clinical Trial Comparing N-Butyl Cyanoacrylate, Radiofrequency Ablation and Endovenous Laser Ablation for the Treatment of Superficial Venous Incompetence: Two Year Follow up Results. Eur J Vasc Endovasc Surg, 2018 Jul 26;56(4). PMID 30042039


34. Morrison, NN, Kolluri, RR, Vasquez, MM, Madsen, MM, Jones, AA, Gibson, KK. Comparison of cyanoacrylate closure and radiofrequency ablation for the treatment of incompetent great saphenous veins: 36-Month outcomes of the VeClose randomized controlled trial. Phlebology, 2018 Nov 8;26835555818810259:268355518810259. PMID 30403154


**Other References:**
2. Blue Cross and Blue Shield of Kansas board certified vascular surgeon medical consultant (481), January 2009.