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Varicose Vein Management

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Related Policies (if applicable)
SUR701.015: for Therapeutic Embolization and Vessel Occlusion to Treat Pelvic Conditions

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Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

NOTE 1: Refer to medical policy SUR701.015 for Therapeutic Embolization and Vessel Occlusion to Treat Pelvic Conditions.

Symptoms of Varicose Vein Insufficiency
Any surgical treatment for varicose veins requires, at a minimum, that the individual is symptomatic with one or more of the following symptoms:

1. Persistent aching/pain, cramping, burning, itching, swelling, or other symptoms significantly interfering with activities of daily living;
2. Significant and/or recurrent episodes of superficial phlebitis;
3. Bleeding from a varicosity;
4. Refractory dependent edema;
5. Ulceration from venous stasis;
6. Stasis dermatitis and its variations (e.g., lipodermatosclerosis).

I. ENDOVASCULAR AND OPEN VEIN PROCEDURES

For the following veins:
a) Greater saphenous vein (GSV),
b) Duplicate greater saphenous vein (GSV) (See **NOTE 2** below),
c) Small saphenous vein (SSV),
d) Anterior accessory and posterior accessory great saphenous veins, and/or
e) Perforator veins;

The following procedures:
a) Vein high ligation, division and stripping,
b) Subfascial endoscopic perforator surgery (SEPS),
c) Endoluminal radiofrequency ablation (ERFA or ERA),
d) Endoluminal venous laser ablation (ELA or EVLT),
e) Truncal ablation with cyanoacrylate (VenaSeal), excluding perforators,
f) Truncal ablation with stabilized microfoam (Varithena), excluding use on small saphenous veins (SSV) and/or perforators.

May be considered medically necessary when **ALL** the following conditions are met:
1. The individual is symptomatic with one or more of the symptoms of varicose vein insufficiency (listed above); AND
2. A duplex Doppler and/or spectral flow ultrasound study, performed within the last 12 months, in the upright or reverse Trendelenburg position documents **ALL** the following:
   a) The specific vein(s) that will be treated; AND
   b) Vein size equal to or greater than 3 mm throughout the length of the vein to be treated; AND
   c) The anatomical classification/location of the vein(s) to be treated; AND
   d) High volume reflux with significant venous insufficiency as manifested by outward flow lasting more than 500 milliseconds or a venous filling index >7 ml/sec in either the saphenous veins or the perforating veins throughout the segment to be treated (reflux in the saphenofemoral junction alone does not qualify for treatment); AND
3. The individual has clinical findings consistent with:
   a) Class 2 or 3 on the CEAP Clinical Findings table as shown below, and has followed a program of conservative treatment *(*** See EXCEPTION #1***) for a minimum of six (6) weeks of compression stockings, walking, leg elevation when possible, analgesics or non-steroidal anti-inflammatory Drugs (NSAIDs); OR
   b) Class 4, 4a, 4b, 4c, 5, 6 or 6r on the CEAP Clinical Findings table 1. (Photos may be required.)

CEAP Clinical Findings (Clinical, Etiologic, Anatomic and Pathophysiologic) Classification of Chronic Venous Disease of the Lower Extremities:	
C0	No visible or palpable signs of venous disease.
C1	Telangiectasias or reticular veins.
C2	Varicose veins.
C2r	Recurrent varicose veins.
C3	Edema.

C4	Changes in skin and subcutaneous tissue secondary to chronic venous disease.
C4a	Pigmentation and eczema.
C4b	Lipodermatosclerosis and atrophie blanche.
C4c	Corona phlebectatica.
C5	Healed venous ulcer.
C6	Active venous ulcer.
C6r	Recurrent active venous ulcer.

**** EXCEPTION #1:*** Only one period of conservative treatment, occurring within the preceding 12 months, is required prior to initial surgical therapy, even when multiple modalities are used for the same individual (e.g., ELA followed by sclerotherapy).

NOTE 2: Duplicate GSV and true duplicate GSV systems are a rare occurrence. The duplicate GSV system will lie in the same plane, parallel to the skin, and run along the aponeurotic deep fascia. These two GSVs will also have the same diameter draining a common cutaneous territory. An anterior accessory vein (AASV) is often mistaken for a duplication of the GSV, but the AASV is usually smaller and does not drain the same cutaneous territory as the GSV. A true duplicate GSV is not an accessory vein and should be treated as any other GSV. Image documentation of a true duplication may be required. Unless a true duplicate, a separate ablation is not necessary.

NOTE 3:

- When stabilized microfoam ablation (Varithena) is used for truncal vein ablation CPT 36465 is used for a single vein treated in a leg and CPT 36466 is used when more than one vein is treated in the same leg on the same day.
- When Varithena is used for sclerotherapy to treat non-truncal veins, CPT 36470 is used for a single vein in a single leg and CPT 36471 is used when more than one vein is treated in the same leg on the same day.

NOTE 4: TREATMENT SESSION LIMITS

1. These procedures are limited to one session for EACH greater saphenous vein, and one session for EACH lesser saphenous vein, and one session for EACH accessory vein, and one session for ALL the perforator veins in EACH leg for a maximum of FIVE sessions per leg, during a period of 12 months. (Great saphenous vein [GSV], Small saphenous vein [SSV], anterior accessory great saphenous vein [AAGSV], posterior accessory great saphenous vein [PAGSV], perforators)
2. A treatment session is a date of service on which one or more truncal veins are treated. For truncal veins like the GSV, SSV, AAGSV, or PAGSV, each vein treated on a given date of service counts against the one ablation per truncal vein per year limit for that specific vein only. You can do more than one truncal vein in the same treatment session on the same date of service.

3. If an ablation (such as RFA or EVLA) is performed on a truncal vein, then a second procedure (such as VenaSeal or Varithena) may not be performed on the same truncal vein within a 12-month period.
4. Requests for treatment extending beyond the initial session limits during a 12-month period will be subject to a new medical necessity review, including submission of all materials normally required for an initial review. Treatment within the initial 12-month period will only be considered with documented evidence of ablation failure.

II. PHLEBECTOMY

Stab avulsion, hook phlebectomy, or transilluminated powered phlebectomy **may be considered medically necessary** when **ALL** the following conditions are met:

1. The individual is symptomatic with one or more of the symptoms of varicose vein insufficiency (listed above); AND
   a) A duplex Doppler and/or spectral flow ultrasound study, performed within the last 12 months, in the upright or reverse Trendelenburg position; AND
2. The individual has clinical findings consistent with:
   a) Class 2 or 3 on the CEAP Clinical Findings table, and has followed a program of conservative treatment *(***see EXCEPTION #2**)* for a minimum of six (6) weeks, consisting of compression stockings, walking, leg elevation when possible, analgesics or NSAIDs; or
   b) Class 4, 4a, 4b, 4c, 5, 6, or 6r on the CEAP Clinical Findings table. (Photos may be required); AND
   c) There is no incompetence in the saphenous veins. This requirement does not have to be met if phlebectomy is performed concurrently with an ablation of a saphenous vein.

CEAP Clinical Findings (Clinical, Etiologic, Anatomic and Pathophysiologic) Classification of Chronic Venous Disease of the Lower Extremities:	
C0	No visible or palpable signs of venous disease.
C1	Telangiectasias or reticular veins.
C2	Varicose veins.
C2r	Recurrent varicose veins.
C3	Edema.
C4	Changes in skin and subcutaneous tissue secondary to chronic venous disease.
C4a	Pigmentation and eczema.
C4b	Lipodermatosclerosis and atrophie blanche.
C4c	Corona phlebectatica.
C5	Healed venous ulcer.
C6	Active venous ulcer.
C6r	Recurrent active venous ulcer.

**** EXCEPTION #2:*** Only one period of conservative treatment, occurring within the preceding 12 months, is required prior to initial surgical therapy, even when multiple modalities are used for the same individual (e.g., ELA followed by sclerotherapy).

NOTE 5: TREATMENT SESSION LIMITS
Requests for treatment extending beyond the initial session limits during a 12-month period will be subject to a new medical necessity review, including submission of all materials normally required for an initial review.

III. SCLEROTHERAPY
Sclerotherapy of the greater saphenous vein (GSV), small saphenous vein (SSV), and GSV/SSV accessory veins, either as a separate procedure or as an adjunct to the procedures described in Section I, **may be considered medically necessary** when **ALL** the following conditions are met:

1. The individual is symptomatic with one or more of the symptoms of varicose vein insufficiency (listed above); AND
2. A duplex Doppler and/or spectral flow ultrasound study, performed within the last 12 months, in the upright or reverse Trendelenburg position, documents **ALL** the following:
   a) Vein size equal to or greater than 3mm; AND
   b) The anatomical classification/location of the vein(s) to be treated; AND
   c) High volume reflux with significant venous insufficiency as manifested by outward flow lasting more than 500 milliseconds or a venous filling index >7 ml/sec in either the saphenous veins or the perforating veins; AND
3. The individual has clinical findings consistent with:
   a) Class 2 or 3 on the CEAP Clinical Findings table as shown below, and has followed a program of conservative treatment (**** See EXCEPTION #3***) for a minimum of six (6) weeks, consisting of compression stockings, walking, leg elevation when possible, analgesics or NSAIDs; OR
   b) Class 4, 4a, 4b, 4c, 5, 6, or 6r on the CEAP Clinical Findings table. (Photos may be required.)

CEAP Clinical Findings (Clinical, Etiologic, Anatomic and Pathophysiologic) Classification of Chronic Venous Disease of the Lower Extremities:	
C0	No visible or palpable signs of venous disease.
C1	Telangiectasias or reticular veins.
C2	Varicose veins.
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C3	Edema.
C4	Changes in skin and subcutaneous tissue secondary to chronic venous disease.
C4a	Pigmentation and eczema.
C4b	Lipodermatosclerosis and atrophie blanche.
C4c	Corona phlebectatica.
C5	Healed venous ulcer.
C6	Active venous ulcer.
C6r	Recurrent active venous ulcer.

Sclerotherapy of the saphenous tributaries **may be considered medically necessary** when **ALL** the following conditions are met:

1. The individual is symptomatic with one or more of the symptoms of varicose vein insufficiency (listed above); AND
2. A duplex doppler and/or spectral flow ultrasound study, performed within the last 12 months, in the upright or reverse Trendelenburg position, documents **ALL** the following:
   a) The anatomical classification/location of the vein(s) to be treated; AND
   b) The size of the vein(s) to be treated; AND
   c) The doppler or duplex report confirms vein size equal to or greater than 3mm; AND
   d) Reflux with significant venous insufficiency is present as manifested by outward flow lasting more than 500 milliseconds; AND
   e) There is **no saphenous** incompetence in the area to be treated (*see ***EXCEPTION #4);*** AND
3. The individual has clinical findings consistent with**:**
   a) Class 2 or 3 on the CEAP Clinical Findings table, and has followed a program of conservative treatment (***see ***EXCEPTION #3***) for a minimum of six (6) weeks, consisting of compression stockings, walking, leg elevation when possible, analgesics or NSAIDs; OR
   b) Class 4, 4a, 4b, 4c, 5, 6, or 6r on the CEP Clinical Findings table. (Photos may be required.)

**** EXCEPTION #3:*** Only one period of conservative treatment, occurring within the preceding 12 months, is required prior to initial surgical therapy, even when multiple modalities are used for the same individual (e.g., ELA followed by sclerotherapy).

**** EXCEPTION #4:*** If sclerotherapy is performed at the same time as an endovascular or open vein procedure (see section I), Doppler requirement does not need to be met for the sclerotherapy.

NOTE 6:

- When stabilized microfoam ablation (Varithena) is used for truncal vein (i.e., great saphenous vein [GSV], anterior accessory saphenous vein [AASV], posterior accessory saphenous vein [PASV]) ablation, CPT 36465 is used for a single vein treated in a leg and CPT 36466 is used when more than one vein is treated in the same leg on the same day.
- When Varithena is used for sclerotherapy to treat non-truncal veins CPT 36470 is used for a single vein in a single leg and CPT 36471 is used when more than one vein is treated in the same leg on the same day.

NOTE 7: TREATMENT SESSION LIMITS

1. Coverage for sclerotherapy for these indications is limited to **a maximum of three (3)** sclerotherapy treatment sessions per leg for the saphenous tributaries when performed within 12 months of the initial invasive varicose vein procedure.
2. Requests for treatment sessions extending beyond one year from the initial invasive treatment session will be similarly subject to a new medical necessity review, including submission of all materials normally required for an initial review.

Sclerotherapy is considered cosmetic for **ANY** of the following:

1. Superficial veins <1 mm in diameter;
2. Varicosities or reticular veins between 1 and <3 mm in diameter;
3. Small congenital vascular malformations with predominantly venous varicosities;
4. To improve the appearance of a non-symptomatic leg.

Compressive isolated sclerotherapy for large, extensive or truncal varicosities **is considered not medically necessary** without ligation of the greater saphenous vein (GSV) at the saphenofemoral junction, or the lesser saphenous vein at the saphenopopliteal junction.

Sclerotherapy of isolated tributary and/or perforator veins without prior or concurrent treatment of saphenous veins **is considered experimental, investigational and/or unproven** when the above criteria are not met.

IV. OTHER

The following techniques for the treatment of varicose veins **are considered experimental, investigational and/or unproven**:

- Endovenous cryoablation;
- Endovenous catheter directed chemical ablation with balloon isolation;
- Mechanochemical ablation (e.g., ClariVein®).

Surgical treatment of varicose veins with clinical findings consistent with CEAP Class 1 (e.g., spider veins and telangiectasia) by **ANY** method **is considered cosmetic.**

Policy Guidelines

For endovenous ablation procedures on perforators, CPT 36475/36478 is used for the first perforator treated and 36476/36479 is used for ALL other perforators treated in the same leg in the same sitting on the same date of service. Therefore, treatment session and date of service are interchangeable in the case of perforators.

Description

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 veins and/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 venous pressure in the deep system is generally greater than that of the superficial system, valve incompetence at any level may lead to backflow (venous reflux) with pooling of blood in superficial veins. Varicose veins with visible varicosities may be the only sign of venous reflux, although itching, heaviness, tension, and pain may also occur. Chronic venous insufficiency secondary to venous reflux can lead to thrombophlebitis, leg ulcerations, and

hemorrhage. The CEAP classification of venous disease considers the clinical, etiologic, anatomic, and pathologic characteristics of venous insufficiency, ranging from class 0 (no visible sign of disease) to class 6 (active ulceration).

Treatment

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

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, compression, and wound care when indicated. Conventional surgical treatment consists of identifying and correcting the site of reflux by ligation of the incompetent junction followed by stripping of the vein to redirect venous flow through veins with intact valves. While most venous reflux is secondary to incompetent valves at the saphenofemoral or saphenopopliteal junctions, reflux may also occur at incompetent valves in the perforator veins or the deep venous system. The competence of any single valve is not static and may be pressure dependent. For example, accessory saphenous veins may have independent saphenofemoral or saphenopopliteal junctions that become incompetent when the great or small saphenous veins are eliminated, and blood flow is diverted through the accessory veins.

Treatment of Saphenous Veins and Tributaries

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

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

Minimally invasive alternatives to ligation and stripping have been investigated. These include sclerotherapy, CAC, and thermal ablation using cryotherapy, high-frequency radio waves (200-300 kilohertz), 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 within 1 to 2 centimeters (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 (GSV) under ultrasound guidance. The laser is then activated and slowly removed, along the course of the saphenous vein. Cryoablation uses extreme cold. The objective of endovenous techniques is to injure the vessel, causing retraction and subsequent fibrotic occlusion of the vein. Technical developments since thermal ablation procedures were initially introduced include the use of perivenous tumescent anesthesia, which allows successful treatment of veins larger than 12 millimeters (mm) in diameter and helps to protect adjacent tissue from thermal damage during treatment of the small saphenous vein (SSV).

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

Endovenous Catheter Directed Chemical Ablation with Balloon Isolation
The KAVS (catheter-assisted vein sclerotherapy) procedure involves an intravascular catheter that is introduced into the vein for short-term therapeutic use. The catheter has a balloon at the distal end that when expanded, will temporarily block the blood flow to that segment of the vein being targeted for sclerotherapy. (1)

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

Cyanoacrylate Adhesive (CAC; e.g., VenaSeal®)
CAC adhesive is a clear, free-flowing liquid that polymerizes in the vessel via an anionic mechanism (i.e., polymerizes into a solid material on contact with body fluids or tissue). The

adhesive is gradually injected along the length of the vein in conjunction with ultrasound and manual compression. The acute coaptation halts blood flow through the vein until the implanted adhesive becomes fibrotically encapsulated and establishes chronic occlusion of the treated vein. Cyanoacrylate glue has been used as a surgical adhesive and sealant for a variety of indications, including gastrointestinal bleeding, embolization of brain arteriovenous malformations, and surgical incisions or other skin wounds.

Transilluminated Powered Phlebectomy (TIPP)
TIPP is an alternative to stab avulsion or 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.

Subfascial Endoscopic Perforator Surgery (SEPS)
SEPS is a minimally invasive surgical procedure for the treatment of chronic venous insufficiency. Incompetent perforators in the calf are believed to be a contributing factor for leg ulceration(s). SEPS is performed as an alternative to the Linton procedure and is recommended in individuals whom conservative measures have failed. 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. (2, 3)

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 lower extremity superficial truncal veins, such as the great saphenous vein, through endovascular embolization with coaptation. The Venaseal Closure System seals the vein using a cyanoacrolate adhesive agent. The VenaSeal Closure System is intended for use in adults with clinically symptomatic venous reflux diagnosed via duplex ultrasound. FDA product code: PJQ. (4)

In 2013, Varithena® (formerly Varisolve), a sclerosant microfoam made with a proprietary gas mix, was approved by the FDA under a new drug application (205-098) for the treatment of incompetent great saphenous veins, accessory saphenous veins, and visible varicosities of the great saphenous vein above and below the knee. (5)

The following devices were cleared for marketing by the FDA through the 501(k) process for the endovenous treatment of superficial vein reflux:

- In 1999, the VNUS Closure® System, a radiofrequency device, was cleared by the FDA through the 510(k) process for "endovascular coagulation of blood vessels in patients with superficial vein reflux." (6) In 2005, The VNUS RFS® and RFS*Flex®* devices were cleared by the FDA for "use in vessel and tissue coagulation including treatment of incompetent (i.e., refluxing) perforator and tributary veins." (7) In 2010, the modified VNUS Closure*Fast* ™ Intravascular Catheter was cleared by the FDA through the 510(k) process. (8) 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." (9) 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. (10)
- In 2003, the Trivex™ System (InaVein), a device for transilluminated powered phlebectomy (TIPP), 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: DWQ. (11)
- In 2008, the ClariVein® Infusion Catheter (Merit Medical) was cleared by the FDA through the 510(k) process (K071468) for mechanochemical ablation. The FDA determined that this device was substantially equivalent to the Trellis® Infusion System (K013635) and the Slip-Cath® Infusion Catheter (K882796). The system includes an infusion catheter, motor drive, stopcock and syringe, and is intended for the infusion of physician-specified agents in the peripheral vasculature. FDA product code: KRA. (12)

Rationale

This medical policy was created in 1996 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through April 5, 2024.

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

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable

intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (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.

Treatment of Saphenous Veins

Clinical Context and Therapy Purpose

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

Compression Therapy

A Cochrane review by O'Meara et al. (2009) evaluated compression for venous leg ulcers included 39 RCTs with 47 different comparisons. (13) This review was updated in 2012 and included 48 RCTs with 59 different comparisons. (14) Most RCTs were small. Objective measures of healing were the time to complete healing, the proportion of ulcers healed within the trial period (typically 12 weeks), the change in ulcer size, and the rate of change in ulcer size. Evidence from 8 trials indicated that venous ulcers healed more rapidly with compression than without. Findings suggested that multicomponent systems (bandages or stockings) were more effective than single-component compression. Also, multicomponent systems containing an elastic bandage appeared more effective than those composed mainly of inelastic constituents. Although these meta-analyses did not include time to healing, studies included in the review reported that the mean time to ulcer healing was approximately 2 months, while the median time to healing in other reports was 3 to 5 months.

A Cochrane review by Knight Nee Shingler et al. (2021) assessed compression stockings as an initial treatment for varicose veins in patients without venous ulceration. (15) This is the second update of a review first published in 2011. Thirteen studies involving 1021 participants with varicose veins without healed or active venous ulceration (CEAP [Clinical, Etiology, Anatomy, Pathophysiology] class C2 to C4) were selected. Compression ranged from 10 to 50 mmHg among studies. Studies could not be pooled for analysis due to heterogeneity in outcomes and method of assessment leading to a low or very low certainty of evidence. Using compression stockings compared to no treatment or placebo stockings led to subjective improvement in symptoms but this finding could be biased because the change in symptoms was not compared to the control arm in all studies. Studies that compared different compression stockings also found subjective improvement in symptoms from baseline to the end of the study, but the change in symptoms was not always compared between groups. The authors were unable to make conclusions about the optimal stocking pressure or length of stocking exposure from the included studies. Reviewers concluded that there was insufficient high-quality evidence to determine whether compression stockings were effective as the sole and initial treatment of

varicose veins in patients without venous ulceration, or whether any type of stocking was superior to another type.

Ligation and Stripping

Systematic literature reviews have indicated a similar healing rate of venous ulcers with superficial vein surgery and conservative compression treatments but a reduction in ulcer recurrence rate with surgery. (16, 17) 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. (18) 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. (19) At 2 years, Doppler ultrasound demonstrated reflux in approximately 10% of patients after ligation and stripping, increasing to 15% at 3 years.

Alternatives to Ligation and Stripping

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

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

Populations

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

Interventions

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

Comparators

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

Outcomes

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

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

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Endovenous Thermal Ablation (Laser or Radiofrequency)

Systematic Reviews

Farah et al. (2022) conducted a systematic review and meta-analysis that informed the 2022 multiorganizational guideline on management of varicose veins. (20) The review addressed 3 key questions related to treatment: whether there is a benefit of surgical stripping versus endovenous ablation, whether there is a benefit of thermal versus nonthermal ablation techniques, and whether ablation of incompetent perforator veins improves outcomes. Multiple outcomes of interest were assessed at various time points for each question. For the first key question, an analysis of 30 RCTs and 16 observational studies found few studies that reported the outcomes of interest at each time point (between 1 month and 5 years), but anatomic closure was better with surgical stripping compared to endovenous ablation techniques. Analysis for the second question included 16 RCTs and 11 observational studies, few of which included the outcomes of interest at the time points of interest. Overall, endovenous laser ablation (EVLA) resulted in higher rates of anatomical closure at 1 year and 5 years versus nonthermal ablation techniques.

A Cochrane review by Whing et al. (2021) compared interventions for GSV incompetence. (21) The review included 24 RCTs (N=5135) and the duration of follow-up for included trials ranged from 5 weeks to 8 years. When comparing EVLA to ligation and stripping, pooled data from 6

RCTs (n=1051) suggest that technical success may be better with EVLA up to 5 years (odds ratio [OR], 2.31, 95% confidence interval [CI], 1.27 to 4.23; low-certainty evidence), but not at 5 years and beyond based on data from 5 RCTs (n=874). The risk of recurrence is similar between treatments within 3 years and at 5 years based on data from 7 RCTs each (n=1459 and n=1267, respectively). When comparing radiofrequency ablation (RFA) to ligation and stripping, data from 2 RCTs (n=318) suggest that there is no significant difference in the rate of technical success up to 5 years; data from 1 RCT (n=289) with duration over 5 years also suggest no significant difference between treatments. Based on data from 4 RCTs (n=546), there is no significant difference in the risk of recurrence up to 3 years; but based on 1 trial (n=289), a possible long-term benefit for RFA is observed (OR, 0.41, 95% CI, 0.22 to 0.75; low-certainty evidence). When comparing EVLA with RFA, technical success is comparable up to 5 years and over 5 years. Based on data from 1 study (n=291), there is no significant difference in the risk of recurrence between treatments at 3 years, but a benefit for RFA over EVLA may be seen at 5 years (OR, 2.77, 95% CI, 1.52 to 5.06).

A Cochrane review by Paravastu et al. (2016) compared EVLA or RFA with surgical repair for small saphenous veins (SSV) with reflux at the saphenopopliteal junction. (22) Three RCTs identified compared EVLA with surgery. There was moderate-quality evidence that recanalization or persistence of reflux at 6 weeks occurred less frequently after EVLA 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 EVLA at 1 year. (OR=0.24; 95% CI, 0.07 to 0.77).

Randomized Controlled Trials

The largest RCT was reported by Brittenden et al. (2014) and compared foam sclerotherapy, EVLA, and surgical treatment in 798 patients. (23) The trial was funded by the United Kingdom (U.K.) 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 EVLA 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 Randomized Study Comparing EVLA with Crossectomy and Stripping of the GSV study (RELACS) randomized 400 patients to EVLA performed by a surgeon at 1 site or to ligation and stripping performed by a different surgeon at a second location. (24) At 2-year follow-up, there were no significant differences between groups for clinically recurrent varicose veins, medical condition measured on the Homburg Varicose Vein Severity Score, or disease-related QOL. Saphenofemoral reflux was detected by ultrasonography more frequently after endovenous laser treatment (17.8% vs 1.3%). The follow-up rate at 5 years was 81%. (25) Same-site recurrences were more frequent in the EVLA group (18% with EVLA 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 EVLA, 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 5 years.

Christenson et al. (2010) compared EVLA with ligation and stripping in 200 limbs (100 in each group). (26) At 1-year follow-up, 98% of the limbs were reported to be free of symptoms. At 2-year follow-up, the EVLA group had 2 veins completely reopened and 5 partially reopened, which was significantly greater than in the ligation and stripping group. In the 2013 Comparative Study of the Treatment of Insufficient GSV: Surgery vs Ultrasound Guided Sclerotherapy with Foam and Endovenous Laser Therapy (MAGNA) trial, 223 consecutive patients (240 legs) with GSV reflux were randomized to EVLA, ligation and stripping, or foam sclerotherapy. (27) At 1-year follow-up, the anatomic success rates were similar between EVLA (88.5%) and stripping (88.2%), which were both superior to foam sclerotherapy (72.2%). Ten percent of the stripping group showed neovascularization. At 5 years, health related QOL and CEAP classification improved in all groups with no significant differences among them. (28) 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 EVLA (13%) groups.

Wallace et al. (2018) published the 5-year outcomes of an RCT consisting of EVLA compared with conventional surgery as treatment for symptomatic great saphenous varicose veins. (29) 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 ($p=0.074$).

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

Table 1. Summary of Key RCT Characteristics

Study; Trial	**Countries**	**Sites**	**Dates**	**Participants**	**Interventions**	
					Active	**Comparator**
Brittenden (2014); (23)	U.K.	11	2008-2012	Individuals with primary varicose veins.	Foam sclero-therapy (n=286) or EVLA (n=210).	Surgical treatment (n=289).
Rass (2012); (24, 25), RELACS	U.S.	2	2004-2007	Individuals with GSV Insufficiency.	EVLA (n=185).	Surgical treatment (n=161).

Wallace (2018); (29)	U.K.	1	2004-2009[1]	Individuals with GSV Insufficiency.	EVLA (n=108).	Surgical treatment (n=110).

n: number; RELACS: Randomized Study Comparing Endovenous Laser Ablation with Crossectomy and Stripping of the Great Saphenous Vein; RCT: randomized controlled trial; GSV: great saphenous vein; EVLA: endovenous laser ablation; UK: United Kingdom; U.S.: United States.
[1] Date of original intervention study.

Table 2. Summary of Key RCT Results

Study	AVVQ Score at Baseline; 6 Months	Frequency of Procedural Complications	Rate of Same-Site Recurrence	Clinically Recurrent Varicose Veins	AVVQ Score at Baseline; 5 years
Brittenden (2014) (23)					
Foam	17.69.9; 9.17.9	6%			
Laser	17.89.1; 7.98.4	1%			
Surgery	18.29.1; 7.87.5	7%			
P-value		<0.001			
Rass (2012) RELACS (24, 25)					
Laser			18%	16.2%	
Surgery			5%	23.1%	
P-value			0.002	0.15	
Wallace (2018) (29)					
Laser				20.9%	13.69; 4.59
Surgery				34.3%	12.73; 3.35
P-value				0.010	<0.001

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

The literature on the isolated treatment of the anterior accessory saphenous vein is relatively limited. A systematic review by Alozai et al. (2021) identified 16 studies that evaluated treatment modalities for anterior accessory saphenous vein incompetence. (30) All included studies were of moderate to poor quality. The pooled anatomic success rates were 91.8% after EVLA and RFA (n=11 studies), 93.6% after CAC (n=3 studies), and 79.8% after sclerotherapy (n=2 studies).

Subsection Summary: Endovenous Thermal Ablation (Laser or Radiofrequency)
There are multiple large RCTs and systematic reviews of RCTs assessing endovenous ablation using radiofrequency or laser energy of the saphenous veins. Comparison with ligation and stripping at 2 to 5-year follow-up has indicated similar recurrence rates for the different

treatments. Evidence has suggested that ligation and stripping may lead to neovascularization, while thermal ablation may lead to recanalization, resulting in similar outcomes for endovenous thermal ablation and surgery. Laser ablation and RFA have similar success rates.

Sclerotherapy

A Cochrane review by Whing et al. (2021) compared interventions for GSV incompetence. (21) Based on pooled data from 4 RCTs (n=954), ultrasound-guided foam sclerotherapy was inferior to ligation and stripping for technical success up to 5 years (OR, 0.32, 95% CI, 0.11 to 0.94; low-certainty evidence), and beyond 5 years based on 3 RCTs (n=525) (OR, 0.09, 95% CI, 0.03 to 0.30; moderate-certainty evidence). There was no significant difference between treatments for recurrence up to 3 years based on 3 RCTs (n=822) and beyond 5 years based on 3 RCTs (n=639). Similarly, technical success was improved with EVLA over ultrasound-guided foam sclerotherapy up to 5 years based on data from 3 RCTs (n=588) (OR, 6.13, 95% CI, 0.98 to 38.27; low-certainty evidence), and beyond 5 years based on data from 3 RCTs (n=534) (OR, 6.47, 95% CI, 2.60 to 16.10; low- certainty evidence). There was no significant difference between EVLA and ultrasound-guided foam sclerotherapy for recurrence up to 3 years based on data from 2 RCTs (n=443), and at 5 years based on data from 2 RCTs (n=418).

Hamann et al. (2017) conducted a meta-analysis of RCTs reporting 5-year follow-up. (31) The meta-analysis (3 RCTs, 10 follow-up studies) included 611 legs treated with EVLA, 549 treated with high ligation and stripping, 121 with sclerotherapy, and 114 with high ligation and EVLA. 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 ($p<0.001$).

Physician-Compounded Sclerotherapy

In the 2013 MAGNA trial, 223 consecutive patients (240 legs) with GSV reflux were randomized to EVLA, ligation and stripping, or physician compounded foam sclerotherapy (1 milliliter [mL] aethoxysclerol 3%: 3 cc air). (27) At 1-year follow-up, the anatomic success rate of foam sclerotherapy (72.2%) was inferior to both EVLA (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 GSV 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 EVLA. (28) Thirty-two percent of legs treated initially with sclerotherapy required 1 or more reinterventions during follow-up compared with 10% in the conventional surgery and EVLA groups. However, clinically relevant grade II neovascularization was higher in the conventional surgery (17%) and EVLA (13%) groups than in the sclerotherapy group (4%). EQ-5D scores improved equally in all groups.

Vähäaho et al. (2019) published a study looking at the 5-year follow-up of patients with symptomatic GSV insufficiency. (32) 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 nonstandardized foam application.

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

A noninferiority trial by Shadid et al. (2012) compared foam sclerotherapy with ligation and stripping in 430 patients. (34) The analysis was per protocol. Forty (17%) patients had repeat sclerotherapy. At 2 years, the probability of clinical recurrence was similar in both groups (11.3% sclerotherapy vs 9.0% ligation and stripping), although reflux was significantly more frequent in the sclerotherapy group (35% vs 21%). Thrombophlebitis occurred in 7.4% of patients after sclerotherapy. Two serious adverse events in the sclerotherapy group (deep venous thrombosis, pulmonary emboli) occurred within 1 week of treatment. Lam et al. (2018) reported 8-year follow-up with 53% of the patients in the original trial. (35) All measures of treatment success (e.g., 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 microfoam (Varithena®) was approved under a new drug application for the treatment of varicose veins. Efficacy data was derived from 2 randomized, blinded, multicenter studies. (5) One compared polidocanol at 0.5%, 1.0%, and 2.0% with endovenous placebo or a subtherapeutic dose of polidocanol foam. The primary endpoint was an improvement in symptoms at week 8, as measured by the Varicose Vein Symptoms Questionnaire. The improvement in symptoms was greater in the pooled polidocanol treatment group (p<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. The second study, VANISH-2, was published by Todd et al. (2014). (36) At the 8-week assessment, there was the 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 EVLA or stripping. A randomized trial comparing EVLA and stripping with this new preparation of foam sclerotherapy is needed to evaluate its comparative effectiveness. Evaluation out to 5 years is continuing.

Vasquez et al. (2017) reported on a double-blind RCT that evaluated the addition of polidocanol microfoam to endovenous thermal ablation. (37) A total of 17 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 polidocanol versus 23.7% for placebo, p=0.037).

Deak (2018) reported a retrospective review of 250 patients with symptomatic chronic venous insufficiency who were treated with polidocanol microfoam in a community practice. (38) Patients who had tortuous veins that were not accessible with a catheter or who had a history of a previous vein ablation procedure with scarring in the lumen were selected for treatment with the microfoam scleroscent. It was reported that some patients required additional treatments between 5 days and 2 years for the vein to close, but the publication did not report how many additional treatments were given. After all the treatments were completed, 94.4% of patients showed elimination of venous valvular reflux and symptom improvement in this chart review. In addition to the lack of information on the number of treatments given, the time of patient follow-up was variable (from 1 month to 2 years), precluding any conclusions regarding the durability of the treatment.

Endovenous Catheter Directed Chemical Ablation with Balloon Isolation (i.e., KAVS)
Evidence evaluating the long-term safety and efficacy for endovenous catheter directed chemical ablation with balloon isolation for varicose veins (i.e., KAVS catheter-assisted vein sclerotherapy) has not been published in the peer reviewed literature. In theory, adding occlusive balloon isolation to the vein wall may enhance the interaction of the sclerosant although evidence is insufficient in determining KAVS improves net outcomes.

Subsection Summary: Sclerotherapy
In a Cochrane review, ultrasound-guided foam sclerotherapy was inferior to ligation and stripping and EVLA for technical success up to 5 years and beyond 5 years, but there was no

significant difference between treatments for recurrence up to 3 years and at 5 years. For physician-compounded sclerotherapy, there is high variability in success rates of the procedure and some reports of serious adverse events. Results of a noninferiority trial of physician-compounded sclerotherapy indicated that once occluded, recurrence rates at 2 years are similar to those of ligation and stripping. By comparison, rates of occlusion with the FDA-approved microfoam sclerotherapy (polidocanol 1%) are similar to those for EVLA or stripping.

In addition, there is no long-term data available to demonstrate the safety and efficacy for endovenous catheter directed chemical ablation with balloon isolation for varicose veins (i.e., KAVS catheter-assisted vein sclerotherapy) therefore, this technique is considered experimental, investigational and/or unproven.

Mechanochemical Ablation (MOCA; Clarivein)

Randomized Controlled Trials

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

Two publications (Bootun et al. [2016], Lane et al. [2017]) reported on early results from an RCT of 170 patients that compared ClariVein with RFA. (39, 40) Maximum visual analog scale (VAS) pain scores (out of 100) during the procedure were significantly lower in the MOCA group (median, 15 mm) than in the RFA group (median, 34 mm; p=0.003). Average VAS pain scores during the procedure were also modestly lower in the MOCA group (median, 10 mm) than in the RFA group (median, 19.5 mm; p=0.003). Occlusion rates, clinical severity scores, disease specific QOL, and generic QOL scores were similar between groups at 1 and 6 months. Limitations of this study are described in Tables 5 and 6. Only 71% of patients were available for follow-up at 6 months, limiting the evaluation of closure rates at this time point.

Vähäaho et al. reported an RCT that compared MOCA with endovenous thermal ablation (EVLA or RFA). (32) 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 GSV 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). (39) Therefore, it is uncertain whether the concentration of sclerosant in the study by Vähäaho et al. was optimal (see Table 5).

Three percent polidocanol was tested in the Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation (MARADONA) non-inferiority trial reported by Holewijn et al. (2019). (42) Although the study was powered for 400 participants, only 213 patients were randomized before reimbursement for the procedure was suspended. Pain scores in the 14 days after the procedure were slightly lower, but hyperpigmentation was higher. Anatomic failures were significantly greater in the MOCA group at 1 year and approached significance at 2-years; with

the note that the study was underpowered for anatomic failures because of the early stoppage of the study. At 1 and 2-years, clinical and QOL outcomes were similar in the 2 groups.

A fourth RCT reported by Mohamed et al. (2021) is the ongoing RCT Comparing EVLA and MOCA (ClariVein) in the Management of Superficial Venous Insufficiency (LAMA). (43) Patients (n=150) were randomized to MOCA with 1.5% sodium tetradecyl sulfate or to EVLA. Anatomic success (occlusion) rates were lower in the MOCA group 77% compared to the EVLA group (91%) with no significant difference between the 2 treatments in intraprocedural pain scores. In contrast to the difference in anatomical occlusion rates, clinical severity and QOL scores were not significantly different between the groups at 1-year follow-up. Follow-up is continuing to evaluate durability of the treatments.

Table 3. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Bootun et al. (2016) (39); Lane et al. (2017) (40)				170 patients with varicose veins	MOCA	RFA
Vähäaho et al. (2019) (32)				132 patients with varicose veins	MOCA with 1.5% polidocanol	Thermal ablation (EVLA or RFA)
Holewijn et al. (2019) (42) (MARADONA)	E.U.	4	2012-2015	213 patients with GSV incompetence and CEAP C2-C5	MOCA with 2 mL of 3% polidocanol for the first 10-15 cm and 1.5% polidocanol for the remainder	RFA
Mohamed et al. (2021) (43) LAMA	U.K.	1	2015-2018	150 patients with symptomatic superficial venous incompetence CEAP 2-6	MOCA (n=75) with 1.5% sodium tetradecyl sulfate	EVLA (n=75)

E.U.: European Union; EVLA: endovenous laser ablation; CEAP: clinical etiologic anatomic pathological; GSV: Great saphenous vein; LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation; MOCA:

mechanochemical ablation; RCT: randomized controlled trial; RFA: radiofrequency ablation; U.K.: United Kingdom.

Table 4. Summary of Key RCT Results

Study	**Pain**	**Post-procedure Occlusion Rate**	**Occlusion Rate at Follow-up**	**Clinical Severity**	**Clinical Severity at Follow-up**		**QOL**
Bootun et al. (2016) (39); Lane et al. (2017) (40)	**During procedure – VAS**		**6 month Occlusion Rates**				
N			71%		71%		
MOCA	10mm						
RFA	19.5mm						
p-value	0.003	NS	NS	NS	NS		NS
Vähäaho et al. (2019) (32)			**1 yr.**		**1 yr.**		
N			117 (88.6%)		117 (88.6%)		
MOCA			45 of 55 (82%)				
EVLA or RFA			100%				
p-value			0.002				
Holewijn et al. (2019) (42) MARADONA	**For the 14 days after the procedure median (range)**	**30-day failure rate**	**1 yr. recanalization rate**	**2 yr. recanalization rate**	**1 yr. VCSS**	**2 yr. VCSS**	**AVVQ improved**
N			153 (72%)	157 (73%)	153 (72%)	157 (73%)	
MOCA	0.2 (0.0-0.8)	5 (4.9%)	15 (16.5%)	21 (20%)	1.8	1.0	88%
RFA	0.5 (0.2-1.3)	1 (1%)	5 (5.8%)	12 (11.7%)	1.7	1.0	89%
p-value	0.01	0.10	0.025	0.066	0.695	0.882	0.90
Mohamed et al. (2021) (43) LAMA	**Median (IQR)**		**Occlusion at 1 yr.**		**VCSS**		**AVVQ Median (IQR)**
N			138 (92%)				

MOCA	15 (9-29)		53/69 (77%)				2.0 (0.0-5.3)
EVLA	22 (9-44)		63/69 (91%)				2.0 (0.0-4.8)
p-value	0.21		0.020		NS		NS

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

Table 5. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-up[e]
Bootun et al. (2016) (39); Lane et al. (2017) (40)				1. Primary outcome was pain during the procedure.	1. Outcomes only out to 6 months, which is insufficient to assess durability.
Vähäaho et al. (2019) (32)	4. Strict inclusion criteria that may not be representative of intended use.	3. The concentration of sclerosant (1.5% polidocanol) may not have been optimal.			1. Outcomes only out to 1 year, which is insufficient to assess durability.
Holewijn et al. (2019) (42) MARADONA	4. Patients with bilateral reflux were excluded due to dosing limits of polidocanol.				
Mohamed et al. (2021) (43) LAMA					1. Outcomes out to 1 year; follow-up is continuing.

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

Table 6. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Bootun et al. (2016) (39); Lane et al. (2017) (40)		1. Patients not blinded to treatment (assessors of duplex ultrasound were blinded).		1. 76% follow-up at 1 month and 71% follow-up at 6 months.		
Vähäaho et al. (2019) (32)		1, 2, 3. Patients, surgeons, and assessors were not blinded to treatment.				
Holewijn et al. (2019) (42) MARADONA		1, 2, 3. Patients, surgeons and assessors were not blinded to treatment.			3. Under-powered for anatomic success due to early termination of recruitment.	4. Results of non-inferiority analysis were not reported.

Mohamed et al. (2021) (43) LAMA		1, 2, 3. Patients, surgeons and assessors were not blinded to treatment.				2. 14-day pain scores were not analyzed by repeated measures ANOVA.

ANOVA: analysis of variance; LAMA: A Randomised Clinical Trial Comparing Endovenous Laser Ablation and Mechanochemical Ablation (ClariVein) in the Management of Superficial Venous Insufficiency; MARADONA: Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation

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

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] 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.

Prospective Cohort Studies

A prospective cohort study that had 5-year follow-up was reported by Thierens et al. (2020). (44) Study inclusion criteria are described in Table 7. Anatomic and clinical follow-ups were performed at 4 weeks, 6 months, and 1, 3, and 5 years after the procedure (Table 8). With slightly less than half of the participants remaining in the study through 5 years, 79% had freedom from anatomic failure and clinical measures had worsened. Nearly 15% of the recanalization's occurred in the first year, which the authors considered to be due to technical issues when the procedure was initially introduced. For example, there has been an increase in the concentration of sclerosant over time. It should be noted, however, that the more recent MARADONA trial from the same group of investigators using 3% polidocanol (described above) also saw a rate of recanalization of 16.5% in the first year and 20% in the second year. (42) Without a control condition, it cannot be determined whether the loss of clinical improvement in this cohort study is due to recanalization or the usual progression of venous disease over time.

Table 7. Summary of Prospective Cohort Study Characteristics

Study	Country	Participants	Treatment Delivery	Follow-Up
Thierens et al. (2020) (44)	Netherlands	CEAP C2-C5 varicose veins; GSV diameter of 3-12 mm and primary GSV insufficiency determined by duplex ultrasound examination.	MOCA with 2% polidocanol as sclerosant	5 year

GSV: great saphenous vein; MOCA: mechanochemical ablation; CEAP: clinical etiologic anatomic pathological.

Table 8. Summary of Prospective Cohort Study Results

Outcome Measure	Baseline	1 year	3 year	5 year
Thierens et al. (2020) (44)	N=94	90	71	58
Freedom from anatomic failure (SE)		85.6% (0.33)	80.1% (0.039)	78.7% (0.041)
AVVQ score	8.9	2.3	5.6	6.3
VCSS score	4.0	1.0	1.0	2.0
Clinical improvement		80%	74%	65%

AVVQ: Aberdeen varicose vein questionnaire; MOCA: mechanochemical ablation; SE: standard error; VAS: visual analog scale.; VCSS: venous clinical severity score.

Subsection Summary: Mechanochemical Ablation (MOCA)

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

conducted RCTs is needed to establish the efficacy and durability of this procedure compared with the criterion standard of thermal ablation.

Cyanoacrylate Adhesion (i.e., VenaSeal™)

Randomized Controlled Trials

The VenaSeal pivotal study (VeClose), a multicenter noninferiority trial with 222 patients, compared VenaSeal with RFA for the treatment of venous reflux. The pivotal registration study for the VeClose study and follow-up through 36 months have been published. (4, 45) These reports are summarized in Tables 9 and 10. 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 VCSS 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. (46)

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). (47) Twenty-four-month results were reported by Gibson et al. (2018), which included 171 patients (87 from CAC and 84 from RFA). (48) 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). (49) 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 9). (50) Periprocedural outcomes showed a shorter intervention time, less pain, and shorter return to work with CAC compared to endovenous thermal ablation (see Table 10). There was no significant difference in occlusion rates between the three treatments at 6, 12, and 24-month follow-up.

Alhewy et al. (2024) conducted an RCT at 2 centers in Egypt comparing VenaSeal CAC with RFA in 248 patients with venous reflux, with follow-up extending to 2 years post procedure. (51) The primary outcome was complete closure of the target GSV at the 3-month visit, although results for this outcome were not reported by the authors. Authors reported that at the 1-month follow-up, all veins treated with CAC remained occluded, while 154 out of 158 (97%) veins treated with RFA remained occluded. At 24 months, 122 out of 128 (95%) veins treated with CAC and 146 out of 158 (93%) veins treated with RFA remained occluded. At month 24, there were 6 recanalizations in the CAC group and 12 in the RFA group, with recanalization-free survival in the CAC group found to be non-inferior to that of the RFA group (95.3% vs. 92.4%, respectively; p<.0001 for 10% noninferiority). The CAC group experienced

fewer complications, with only 2 cases of paresthesia and 18 cases of bruises reported, whereas the RFA group encountered 18 cases of bruises, 2 cases of skin burns, and 2 cases of access site hematoma. Periprocedural outcomes showed a potentially shorter intervention time with CAC vs. RFA.

Table 9. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions[2]	
					Active	***Comparator***
FDA SSED (4), Morrison et al. (2015 [45], 2017 [52], 2019 [49]); Gibson et al. (2018) (46) VeClose trial	U.S.	10	2013-2014	Age ≥21 and ≤70 years with symptomatic[1] GSV reflux and CEAP C2-C4b. GSV diameter while standing of 3-12 mm.	108 Venaseal CAC.	114 RFA.
Eroglu and Yasim (2018) (50)	Asia	1	NR	525 patients ≥18 years with incompetence of the GSV (>5.5 mm in diameter) or SSV (>4 mm in diameter) and reflux >0.5 seconds.	175 VariClose CAC.	125 RFA and 125 EVLA.
Alhewy et al. (2024) (51)	Egypt and Saudi Arab	2	August 1, 2018, to May 1, 2022	248 patients ≥18 years (286 limbs) with symptomatic moderate to severe varicosities, CEAP classifications of C2- C5, and GSV incompetence with a reflux time of 0.5 seconds	128 VenaSeal CAC	120 RFA.

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; U.S.: United States.

[1] One or more of the following symptoms related to the target vein: aching, throbbing, heaviness, fatigue, pruritus, night cramps, restlessness, generalized pain or discomfort, swelling.

[2] Protocol mandated use of compression stockings for 7 days post-procedure.

Table 10. Periprocedural Outcomes

	Duration of Procedure minutes (SD)	Average Periprocedural Pain[1]	2 or More Analgesics Used Daily n (%)	1 Day to Return to Work	2 Days to Return to Work	3 or More Days to Return to work
Eroglu and Yasim (2018) (50)						
N	503	503	456	456	456	456
VariClose	15.3 (2.6)	1 (mild)	105 (62.5)	161 (95.8)	7 (4.2)	0 (0)
RFA	27.3 (7.7)	2 (moderate)	98 (65.8)	75 (50.3)	53 (35.6)	21 (14.1)
EVLA	35.0 (5.2)	2 (moderate)	105 (75.5)	105 (75.5)	24 (17.3)	10 (7.2)
p-Value	<0.001		0.1472	<0.0012		
Alhewy et al. (2024) (51)						
N	248					
VenaSeal	range, 25-54					
RFA	Range, 40-70					
p-value	NR					

EVLA: endovenous laser ablation; NR: not reported; RFA: radiofrequency ablation; SD: standard deviation.
[1]Scale of 1 to 4.
[2]Overall p-Value.

Table 11. Summary of Key RCT Results

Study	Vein Closure[1] n (%)	Vein Closure 12 months n (%)	Vein Closure 24 months n (%)	Vein Closure 36 months n (%) or VCSS	Device related Event n (%)
FDA SSED (4), Morrison et al. (45, 52, 49); Gibson et al. (2018) (46) (VeClose trial)	**3 months**	(			
N	222	189	171	146	222
VenaSeal	107 (99.1%)[2]	92 (96.7%)	82/86 (95.3%)	68/72 (94.4%)	31 (27%)
RFA	109 (95.6%)[2]	91 (96.8%)	79/84 (94.0%)	68/74 (91.9%)	7 (6%)

Eroglu and Yasim (2018) (50)	**6 months**			**VCSS at 24 months**	
N		503	456	456	
VariClose	98.1%	94.1%	95.1%	2.7	
RFA	94.7%	92.5%	94.2%	3.7	
EVLA	92.6%	90.9%	91.5%	3.5	
p-Value	NS	NS	NS	<0.001	
Alhewy et al. (2024) (51)	Vein Closure at 1 month				
N	248				
VenaSeal	128/128 (100%)	122/128 (95%)			
RFA	154/158 (97%)	146/158 (93%)			
p-value	NR	NR			

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

Notable limitations of the studies are shown in Tables 12 and 13. The primary limitation of the pivotal study of VenaSeal is the loss to follow-up at 2 and 3 years, although loss to follow-up was similar in the 2 groups. The study by Eroglu and Yasim (2018) had an unequal loss to follow-up after patients were informed of the treatment allocation. (50) 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. The study conducted by Alhewy et al. (2024) presented descriptive results for vein closure outcomes without inclusion of p-values or other statistical outputs. (51) Additionally, the study did not report the results of the prespecified primary outcome.

Table 12. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Morrison et al. (2015 [45], 2017 [52]); Gibson et al. (2018) (48); Morrison et al. (2019) (49) (VeClose Trial)					1. Follow-up will continue to 60 months.

Eroglu and Yasim (2018) (50)		2. This specific cyanoacrylate product is not currently available in the U.S.			
Alhewy et al. (2024) (51)					

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

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

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

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

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

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

Table 13. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statistical[f]
Morrison et al. (2015 [45], 2017 [52]) Gibson et al. (2018) (48); Morrison et al. (2019) (49) [VeClose Trial]		1, 2, 3. The outcome was assessed by the treating physician and patients were not blinded.		1. >20% loss to follow-up.		3. Variable reporting of CI and p values.
Eroglu and Yasim (2018) (50)		1, 2, 3. Patients were notified of the group assignment a day before		6, 7. Not intent-to-treat analysis and unequal loss to		

		the procedure.		follow-up. 21 patients did not receive the allocated intervention, 19 of whom were in the control groups.		
Alhewy et al. (2024) (51)		4. blinding not Reported.			1. power calculations not reported.	3. CI and p values mostly not reported.

CI: confidence interval. The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias, 5. Other.

[b] Blinding key: Not 1. Participants or study staff not blinded; 2. Outcome accessors not blinded; 3. Outcome assessed by treating physician; 4. Other.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials; 7. Other.

[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. 5. Other.

Prospective Cohort Studies

Eroglu and Yasim (2017) reported closure rates of 94.1% at 30 months in a prospective cohort of 159 patients. (53) Thirty-three- month follow-up was reported by Zierau (2015) for 467 (58.7%) of 795 veins treated at 1 institution in Germany. (54) 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.

Subsection Summary: Cyanoacrylate Adhesive (CAC)

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. An RCT (n=525) with an 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.

Cryoablation

Randomized Controlled Trials

Klem et al. (2009) reported on a randomized trial that found endovenous cryoablation (n=249) to be inferior to conventional stripping (n=245) for treating patients with symptomatic varicose veins. (47) Forty-four percent of patients had residual GSV remaining with cryoablation while 15% had residual vein remaining with conventional stripping. The 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 EVLA. (55, 56) Included were 120 patients with symptomatic uncomplicated varicose veins (CEAP class C2) with saphenofemoral incompetence and GSV reflux. At 10 days after treatment, EVLA 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 EVLA 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 EVLA and in 51% of patients treated with cryoablation (p=*NS*). Neovascularization was more common after cryoablation, but incompetent tributaries were more common after EVLA. There were no significant differences between groups in the VCCS or AVVQ scores at either the 2 or 5-month follow-ups for EVLA.

Subsection Summary: Cryoablation

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

Tributary Varicosities

Clinical Context and Therapy Purpose

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

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

Populations

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

Interventions

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

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

Comparators

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

Outcomes

The general outcomes of interest are reductions in symptoms and morbid events, change in disease status, and improvements in 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 following principles:

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

Sclerotherapy and Phlebectomy

Systemic Reviews

Early studies established ligation and stripping as the criterion standard for treating saphenofemoral incompetence based on improved long-term recurrence rates, with sclerotherapy used primarily as an adjunct to treat varicose tributaries. A Cochrane review of 28 studies by de Avlia Oliveira et al. (2021) concluded that there is low certainty evidence that sclerotherapy is effective and safe compared to placebo for treating cosmetic appearance, persistent symptoms, and quality of life concerns related to varicose veins. (57) Evidence was limited or lacking for comparisons of foam with liquid sclerotherapy or other substances, and between concentrations of foam. Sclerotherapy and phlebectomy are considered appropriate in the absence of reflux of the saphenous system (e.g., post or adjunctive treatment to other procedures such as surgery). (58)

Randomized Controlled Trials

El-Sheikha et al. (2014) reported on a small, randomized trial of concomitant or sequential (if needed) phlebectomy following EVLA for varicose veins. (59) 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. (60) 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. (61) 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 (TIPP)

Systematic Reviews

A meta-analysis by Luebke and Brunkwall (2008) included 5 studies that compared TIPP with conventional surgery. (62) Results showed a significant advantage of TIPP over the conventional treatment for number of incisions, mean cosmetic score, and duration of the procedure. However, TIPP also increased the incidence of hematoma and resulted in worse mean pain scores.

Randomized Controlled Trials

Included in the meta-analysis by Luebke and Brunkwall (2008) was an RCT by Chetter et al. (2006) that compared TIPP (n=29) with a multiple stab incision procedure (n=33). (63) A single surgeon performed all but 2 of the procedures, and there was no difference in operating time. Patients treated with TIPP had an average of 5 incisions, compared with 20 for the multiple stab procedure. However, blinded evaluation revealed that bruising or discoloration was higher for the TIPP group at both 1 and 6 weeks postsurgery. At 6 weeks after surgery, patients in the TIPP group showed no improvement in pain (-2 points on the Burford Pain Scale), while patients in the multiple stab incision group had a significant improvement in pain score compared with presurgical baseline (-20 points). Six weeks post-surgery, QOL measures had improved in the multiple stab incision group but not in the TIPP group. Thus, although TIPP required fewer surgical incisions, in this single-center study, it was associated with longer prolonged 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

Perforator veins cross through the fascia and connect the deep and superficial venous systems. Incompetent perforating veins were originally treated with an open surgical procedure, called

the Linton procedure, which involved a long medial calf incision to expose all posterior, medial, and paramedial perforators. While this procedure was associated with healing of ulcers, it was largely abandoned due to a high incidence of wound complications. The Linton procedure was subsequently modified by using a series of perpendicular skin flaps instead of a longitudinal skin flap to provide access to incompetent perforator veins in the lower part of the leg. The modified Linton procedure may occasionally be used to close incompetent perforator veins that cannot be reached by less invasive procedures.

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

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

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

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

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

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

<u>Study Selection Criteria</u>
Methodologically credible studies were selected using the following principles:

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

<u>Systematic Reviews</u>

Giannopoulos et al. (2022) performed a systematic review of percutaneous treatments for pathologic perforating veins. (64) Thirty-five studies met the inclusion criteria (5 double-arm studies and 28 ingle-arm studies). Endovenous laser ablation (with or without microphlebectomy and/or sclerotherapy) was successful within the first 2 weeks after the procedure in 95% of patients. Success rates for RFA (with or without microphlebectomy) were 91% (95% CI, 75% to 99%). Ultrasound-guided sclerotherapy had a success rate of 70% after multiple sessions (95% CI, 53% to 84%). After 12 months of follow-up, occlusion rates were 89%, 77%, and 83% in the 3 groups, respectively. Limitations of the review include heterogeneity of the interventions in the included studies, including adjuvant therapy that could be provided at the investigator's discretion.

Ho et al. (2022) published a systematic review to compare interventions for incompetent perforator veins, including open ligation, SEPS, endovascular laser ablation, ultrasound-guided sclerotherapy, and RFA. (65) A total of 81 studies (N=7010) were identified, and the overall quality of evidence was low to intermediate. Results demonstrated that in the short term (≤ 1 year), efficacy rates for wound healing were 99.9% for ultrasound-guided sclerotherapy, 72.2% for open ligation, and 96.0% for SEPS. For short-term freedom from wound recurrence, the pooled estimate for SEPS was 91.0%; wound recurrence rates were not reported for other interventions.

A systematic literature review by O'Donnell (2008) indicated that there was a lack of evidence on the role of incompetent perforator vein surgery performed in conjunction with superficial saphenous vein surgery. (17) 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 4 trials included 2 level I (large subject population) and 2 level II (small subject population) studies. Two trials combined surgical treatment of the incompetent perforator veins with concurrent or prior treatment of the superficial saphenous veins; the other 2 treated the 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. (66, 67)

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. (68) O'Donnell (2008) discussed additional (lower quality) evidence to suggest deep venous valvular involvement rather than incompetent perforators in venous insufficiency. (17) 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 (SEPS)
A Cochrane review by Lin et al. (2019) evaluated the efficacy of SEPS for the treatment of venous ulcers. (2) They identified 4 RCTs; 2 compared SEPS plus compression with compression

alone (n=208), one compared SEPS with the Linton procedure (n=39), and one compared SEPS plus saphenous vein surgery with saphenous vein surgery alone (n=75). Results are shown in Table 14. The authors concluded that:

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

Table 14. Meta-Analysis Results

Comparator	Ulcer Healing	Ulcer Recurrence	Adverse Events
Compression alone N	196	208	
Risk ratio (95% CI)	1.17 (1.03-1.33)	0.85 (0.26-2.76)	
Linton Procedure N	39	39	39
Risk ratio (95% CI)	0.95 (0.83-1.09)	0.47 (0.12-2.30)	0.04 (0.00-0.60)
Saphenous Vein Surgery	22	75	75
Risk ratio (95% CI)	0.96 (0.64-1.43)	1.03 (0.15-6.91)	2.05 (0.86-4.90)

CI: confidence interval.

In a meta-analysis of SEPS for chronic venous insufficiency, Luebke and Brunkwall (2009) concluded that "its use should not be employed routinely and could only be justified in patients with persistent ulceration thought to be of venous origin, and in whom any superficial reflux has already been ablated and post thrombotic changes excluded." (69) 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 endoscopic perforator surgery in the future."

Retrospective Studies

Lawrence et al. (2020) reported a multicenter retrospective review of 832 consecutive patients who met criteria and were treated for venous leg ulcers in the U.S. (70) Of the 832 patients, 187 were managed with compression alone (75% ulcer healing) and 528 received superficial vein treatment after failure of a mean of 23 months of compression. Of the 528, 344 also underwent ablation of an average of 1.8 perforator veins. Techniques included radiofrequency, laser, and sclerotherapy. The ulcer healing rate was 17% higher in patients treated for perforator reflux (68%) in comparison with superficial vein treatment alone (51%; hazard ratio, 1.619, 95% CI, 1.271 to 2.063), even though the ulcers were larger at baseline. Perforator vein treatment did

not affect recurrence rates in ulcers that had healed. Larger ulcers were associated with reflux in more than 1 level, and deep vein stenting was performed in 95 patients, some in combination with superficial vein treatment and some in combination with both superficial and perforator vein treatment. The ulcer healing rate in patients who underwent all 3 procedures was 87% at 36 months with an ulcer recurrence of 26% at 24 months.

Section Summary: Perforator Reflux

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

Practice Guidelines and Position Statements

American Venous Forum et al.

In 2020, in response to published reports of potentially inappropriate application of venous procedures, the American Venous Forum, Society for Vascular Surgery, American Vein and Lymphatic Society, and the Society of Interventional Radiology published appropriate use criteria for the treatment of chronic lower extremity venous disease. (71) Appropriate use criteria were developed using the RAND/UCLA method incorporating best available evidence and expert opinion.

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

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

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

Society for Vascular Surgery and the American Venous Forum (AVF)

The Society for Vascular Surgery and the AVF published joint clinical practice guidelines in 2011. (72) Table 15 provides the recommendations.

Table 15. Guidelines on Management of Varicose Veins and Associated Chronic Venous Diseases (72)

Recommendation	Grade[a]	SOR	QOE
Compression therapy for venous ulcerations and varicose veins			
Compression therapy is recommended as the primary treatment to aid healing of venous ulceration.	1B	Strong	Moderate
To decrease the recurrence of venous ulcers, ablation of the incompetent superficial veins in addition to compression therapy is recommended.	1A	Strong	High
Use of compression therapy for patients with symptomatic varicose veins is recommended.	2C	Weak	Low
Compression therapy as the primary treatment if the patient is a candidate for saphenous vein ablation is not recommended.	1B	Strong	Moderate
Treatment of the incompetent GSV			
Endovenous thermal ablation (radiofrequency or laser) is recommended over chemical ablation with foam or high ligation and stripping due to reduced convalescence and less pain and morbidity. Cryostripping is a technique that is new in the United States, and it has not been fully evaluated.	1B	Strong	Moderate
Varicose tributaries			
Phlebectomy or sclerotherapy are recommended to treat varicose tributaries.	1B	Strong	Moderate
Transilluminated powered phlebectomy using lower oscillation speeds and extended tumescence is an alternative to traditional phlebectomy.	2C	Weak	Low
Perforating vein incompetence			
Selective treatment of perforating vein incompetence in patients with simple varicose veins is not recommended.	1B	Strong	Moderate

Treatment of pathologic perforating veins (outward flow of ≥500 ms duration, with a diameter of ≥3.5 mm) located underneath healed or active ulcers (CEAP class C5-C6) is recommended.	2B	Weak	Moderate

CEAP: Clinical Etiology Anatomy Pathophysiology; GSV: great saphenous vein; QOE: quality of evidence; SOR: strength of recommendation.

[a] Grading: strong = 1 or weak = 2, based on a level of evidence that is either high quality = A, moderate quality = B, or low quality = C.

The Society for Vascular Surgery, the American Vein and Lymphatic Society (AVLS), and the AVF published a joint clinical practice guideline in 2022 on management of lower extremity varicose veins. (73) The guideline will be published in sections; the first part (published in 2022) focuses on duplex scanning and treatment of superficial truncal reflex. Superficial truncal veins are defined as the GSV, SSV, anterior accessory GSV, and posterior accessory GSV. A summary of the guideline recommendations is provided in Table 16. The second part of the guideline was published in 2023 and focuses on the management of varicose vein patients with compression, treatment with drugs and nutritional supplements, evaluation and treatment of varicose tributaries, superficial venous aneurysms, and management of complications of varicose veins and their treatment. (74) Relevant guideline recommendations regarding the management of varicose veins and varicose tributaries are summarized in Table 17.

Table 16. Summary of Recommended Treatment of Superficial Truncal Reflex

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

Reflux in the GSV - thermal and nonthermal ablation recommended	1B	Strong	Moderate
Reflux in the SSV - thermal and nonthermal ablation recommended	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory GSV – either thermal or nonthermal ablation suggested	2C	Weak	Low
Varicose veins (CEAP class C2)			
Reflux in the GSV or SSV - recommend against concomitant initial ablation and treatment of incompetent perforating veins	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory GSV -recommend against concomitant initial ablation and treatment of incompetent perforating veins	2C	Weak	Low
Persistent or recurrent symptoms after previous complete ablation - treatment of perforating vein incompetence suggested	2C	Weak	Low
Symptomatic reflux and associated varicosities			
Reflux in the GSV or SSV - ablation and concomitant phlebectomy or ultrasound-guided foam sclerotherapy recommended	1C	Strong	Low
Reflux in the anterior accessory or posterior accessory GSV ablation and concomitant phlebectomy or ultrasound-guided foam sclerotherapy suggested	2C	Weak	Low

CEAP: Clinical Etiology Anatomy Pathophysiology; GSV: great saphenous vein; QOE: quality of evidence; QOL: quality of life; SSV: small saphenous vein; SOR: strength of recommendation.

[a] Grading: strong = 1 or weak = 2, based on a level of evidence that is either high quality = A, moderate quality = B, or low quality = C.

[b] Ligation and stripping can be performed if endovenous ablation is not feasible.

Table 17. Summary of Recommendations for Varicose Veins and Varicose Tributaries.

	Grade[a]	SOR	QOE
Endovenous Ablation vs High Ligation and Stripping			
For patients with symptomatic varicose veins and axial reflux in the GSV, who are candidates for intervention, we recommend treatment with endovenous ablation over HL&S of the GSV.	1	Strong	Moderate
For patients with symptomatic varicose veins and axial reflux in the SSV, who are candidates for intervention, we recommend treatment with endovenous ablation over ligation and stripping of the SSV.	1	Strong	Low to very low
For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, who are candidates for intervention, we suggest treatment with endovenous ablation, with additional phlebectomy, if needed, over ligation and stripping of the accessory vein.	2	Weak	Low to very low

For patients with symptomatic varicose veins and axial reflux in the GSV or SSV, we recommend treatment with HL&S of the saphenous vein if technology or expertise in endovenous ablation is not available or if the venous anatomy precludes endovenous treatment.	1	Strong	Moderate
For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV, we suggest treatment with ligation and stripping of the accessory saphenous vein, with additional phlebectomy if needed, if technology or expertise in endovenous ablations is not available or if the venous anatomy precludes endovenous treatment.	2	Weak	Low to very low
For patients with symptomatic varicose veins and axial reflux in the GSV who place a high priority on the long-term outcomes of treatment (QOL and recurrence), we suggest treatment with EVLA, RFA, or HL&S over physician-compounded UGFS, because of long-term improvement of QOL and reduced recurrence.	2	Weak	Moderate
For patients with symptomatic varicose veins and axial reflux in the SSV, we suggest treatment with EVLA, RFA, or ligation and stripping from the knee to the upper or midcalf over physician-compounded UGFS because of long-term improvement of QOL and reduced recurrence.	2	Weak	Low to very low
For patients with symptomatic varicose veins and axial reflux in the AAGSV or PAGSV who place a high priority on the long-term outcomes of treatment (QOL and recurrence), we suggest treatment of the refluxing superficial trunk with endovenous laser ablation, RFA, or HL&S, with additional phlebectomy if needed, over physician-compounded UGFS because of long-term improvement of QOL and reduced recurrence.	2	Weak	Low to very low
Thermal vs nonthermal ablation of superficial truncal veins			
For patients with symptomatic axial reflux of the GSV, we recommend either thermal or nonthermal ablation from the groin to below the knee, depending on the available expertise of the treating physician and the preference of the patient.	1	Strong	Moderate
For patients with symptomatic axial reflux of the SSV, we recommend either thermal or nonthermal ablation from the knee to the upper or midcalf, depending on the available expertise of the treating physician and the preference of the patient.	1	Strong	Low to very low
For patients with symptomatic axial reflux of the AAGSV or PAGSV, we suggest either thermal or nonthermal	2	Weak	Low to very low

ablation, with additional phlebectomy if needed, depending on the available expertise of the treating physician and the preference of the patient.			
Telangiectasias and reticular veins			
For patients with symptomatic telangiectasias and reticular veins, we recommend sclerotherapy with liquid or foam.	1	Strong	Moderate
For patients with symptomatic telangiectasias or reticular veins, we suggest transcutaneous laser treatment if the patient has sclerosant allergy, needle phobia, sclerotherapy failure, or small veins (<1 mm) with telangiectatic matting.	2	Weak	Moderate
Varicose tributaries			
For treatment of symptomatic varicose tributaries, we recommend miniphlebectomy or ultrasound-guided sclerotherapy using PCF or PEM.	1	Strong	Moderate
For treatment of symptomatic varicose tributaries, we suggest transilluminated powered phlebectomy as an alternative treatment for patients with clusters of varicosities by a physician who is trained in the procedure.	2	Weak	Low to very low
Treatment of varicose tributaries concomitant or staged with superficial truncal ablation			
For patients with symptomatic reflux in the GSV or SSV and associated varicosities, we recommend ablation of the refluxing venous trunk and concomitant phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities with PCF or PEM.	1	Strong	Low to very low
For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest simultaneous ablation of the refluxing venous trunk and phlebectomy or UGFS of the varicosities with PCF or PEM.	2	Weak	Low to very low
For patients with symptomatic reflux in the GSV or SSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or UGFS of the varicosities only if anatomical or medical reasons are present. We suggest shared decision-making with the patient regarding the timing of the procedure.	2	Weak	Low to very low
For patients with symptomatic reflux in the AAGSV or PAGSV, we suggest ablation of the refluxing venous trunk and staged phlebectomy or UGFS of the varicosities only if anatomical or medical reasons are present. We suggest shared decision-making with the patient regarding the timing of the procedure.	2	Weak	Low to very low
Ablation of incompetent perforating veins			

For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the GSV or SSV, we recommend against treatment of incompetent perforating veins concomitant with initial ablation of the saphenous veins.	**1**	Strong	Low to very low
For patients with varicose veins (CEAP class C2) who have significant, symptomatic axial reflux of the AAGSV or PAGSV, we suggest against treatment of incompetent perforating veins concomitant with initial ablation of the superficial truncal veins.	2	Weak	Low to very low

AAGSV: anterior accessory great saphenous vein; CEAP: Clinical, Etiologic, Anatomic, Pathophysiologic classification system; EVLA: endovenous laser ablation; GSV: great sapherous vein; HL&S: high ligation and stripping; PCF: physician-compounded foam; PEM: polidocanol endovenous microfoam; PAGSV: posterior accessory great saphenous vein; QOE: quality of evidence; QOL: quality of life; RFA: radiofrequency ablation; SOR: strength of recommendation; SSV: small saphenous vein; UGFS: ultrasound-guided foam sclerotherapy.

[a] Grading: strong = 1 or weak = 2, based on a level of evidence that is either high quality = A, moderate quality = B, or low quality = C.

American Vein and Lymphatic Society

In 2015, the American Vein and Lymphatic Society (AVLS, previously named The American College of Phlebology) published guidelines on the treatment of superficial vein disease. (75)

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

In 2017, the AVL published guidelines on the treatment of refluxing accessory saphenous veins. (48) 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 GSV 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 (NICE)

In 2013, the United Kingdom's NICE updated its guidance on ultrasound-guided foam sclerotherapy for varicose veins. (76) NICE stated that:

- "1.1 Current evidence on the efficacy of ultrasound-guided foam sclerotherapy for varicose veins is adequate. The evidence on safety is adequate, and provided that patients are

warned of the small but significant risks of foam embolization (see section 1.2), this procedure may be used with normal arrangements for clinical governance, consent and audit.

- 1.2 During the consent process, clinicians should inform patients that there are reports of temporary chest tightness, dry cough, headaches and visual disturbance, and rare but significant complications including myocardial infarction, seizures, transient ischaemic attacks and stroke."

In 2016, NICE revised its guidance on endovenous MOCA, 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…." (77)

In 2020, NICE published guidance on the use of cyanoacrylate glue occlusion for varicose veins which states that current evidence supports the safety and efficacy of this procedure given that standard arrangements are in place for clinical governance, consent and audit. This procedure should only be performed by clinicians with appropriate training in this procedure and experienced in the use of venous ultrasound. (78)

European Society for Vascular Surgery

In 2022, the European Society for Vascular Surgery (ESVS) published clinical practice guidelines on the management of chronic venous disease of the lower limbs. (79). Within these guidelines the authors report that for patients with GSV incompetence requiring treatment, CAC should be considered when a non-thermal non-tumescent technique is preferred. The recommendation was defined as Class IIA (weight of evidence/opinion is in favor of usefulness/efficacy) Level of evidence A (data from multiple RCTs or meta-analyses). Regarding MOCA the authors gave a Class IIB recommendation (usefulness is level of Evidence A- data from multiple RCTs or meta-analyses).

Summary of Evidence

Endovenous Thermal Ablation (Radiofrequency or Laser)

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive endovenous thermal ablation (radiofrequency or laser), the evidence includes randomized controlled trials (RCTs) and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life (QOL), and treatment-related morbidity (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 (EVLA) and radiofrequency ablation (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 an improvement in the net health outcome.

Microfoam Sclerotherapy

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive microfoam sclerotherapy, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, change in disease status, morbid events, QOL, and TRM. In a

Cochrane review, ultrasound-guided foam sclerotherapy was inferior to both ligation and stripping and EVLA for technical success up to 5 years and beyond 5 years, but there was no significant difference between treatments for recurrence up to 3 years and at 5 years. For physician-compounded sclerotherapy, there is high variability in success rates and some reports of serious adverse events. By comparison, rates of occlusion with the microfoam sclerotherapy (polidocanol 1%) approved by the Food and Drug Administration (FDA) are similar to those reported for EVLA or stripping. Results of a noninferiority trial of physician-compounded sclerotherapy have indicated that once occluded, recurrence rates at 2 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 an improvement in the net health outcome.

Endovenous Catheter Directed Chemical Ablation with Balloon Isolation (i.e., KAVS)
For individuals with varicose veins/venous insufficiency and saphenous vein reflux who receive endovenous catheter directed chemical ablation with balloon isolation there is no long term published data to support the long-term safety and efficacy of this procedure. Currently, the evidence is insufficient to determine the effects of the technology on health outcomes.

Mechanochemical Ablation (MOCA; ClariVein®)
For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive MOCA, the evidence includes 4 RCTs with 6 months to 2-year results that compared MOCA to thermal ablation, a prospective cohort with follow-up out to 5 years. 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 tumescent anesthesia and may result in less pain during the procedure. Results to date have been mixed regarding a reduction in intraprocedural pain compared to thermal ablation procedures. Occlusion rates at 6 months to 2 years from RCTs indicate lower anatomic success rates compared to thermal ablation, but a difference in clinical outcomes at these early time points has not been observed. Experience with other endoluminal ablation procedures suggests that lower anatomic success in the short term is associated with recanalization and clinical recurrence between 2 to 5 years. The possibility of later clinical recurrence is supported by a prospective cohort study with 5-year follow-up following treatment with MOCA. However, there have been improvements in technique since the cohort study was begun, and clinical progression is frequently observed with venous disease. Because of these limitations, longer follow-up in the more recently conducted RCTs is needed to establish the efficacy and durability of this procedure compared with the criterion standard of thermal ablation. The evidence is insufficient to determine the effects of the technology on health outcome.

Cyanoacrylate Adhesive (CAC; VenaSeal)
For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive Cyanoacrylate (CAC) adhesive, the evidence includes 3 RCTs and a prospective cohort study. 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, 2 RCTs 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. Another RCT (n=248) comparing Venaseal CAC with RFA found similar proportions of vein closures at 24 months with both treatments, with potentially shorter procedure duration with CAC vs. RFA. A third RCT (N=525) with an 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 an improvement in the net health outcome.

Cryoablation

For individuals who have varicose veins/venous insufficiency and saphenous vein reflux who receive cryoablation, the evidence includes RCTs. 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 outcome.

Ablation (Stab Avulsion, Sclerotherapy, or Phlebectomy) of Tributary Vein(s)

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. 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). Transilluminated powered phlebectomy (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 an improvement in the net health outcome.

Ablation (e.g., Subfascial Endoscopic Perforator Surgery) of Perforator Veins

For individuals who have perforator vein reflux who receive ablation (e.g., subfascial endoscopic perforator surgery) of perforator veins, the evidence includes RCTs, systematic reviews of RCTs, and a retrospective study. 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. 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 an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some ongoing and unpublished trials that might influence this policy are listed in Table 18.

Table 18. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05633277	Outcomes of Sclerotherapy of the Ulcer Bed Compared to a Combination of Ablation and Injections	30	Mar 2024
NCT04737941	Finnish Venous Ulcer Study	248	Mar 2026
NCT03820947[a]	Global, Post-Market, Prospective, Multi-Center, Randomized Controlled Trial of the VenaSeal™ Closure System vs. Surgical Stripping or Endothermal Ablation (ETA) for the Treatment of Early & Advanced Stage Superficial Venous Disease	500	Apr 2028
Unpublished			
NCT03392753	Randomised Controlled Trial of Mechanochemical Ablation Versus Cyanoacrylate Adhesive for the Treatment of Varicose Veins	167	Dec 2021
NTR4613[a]	Mechanochemical endovenous ablation versus radiofrequency ablation in the treatment of primary small saphenous vein insufficiency (MESSI trial)	160	Apr 2020

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

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	0524T, 36465, 36466, 36468, 36470, 36471, 36473, 36474, 36475, 36476, 36478, 36479, 36482, 36483, 37500, 37700, 37718, 37722, 37735, 37760, 37761, 37765, 37766, 37780, 37785, 37799, 76942
HCPCS Codes	S2202

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
07/15/2025	Document updated. The following changes were made in Coverage: 1) Clarified treatment session limits in Note 4; and 2) Clarified coding for perforators in policy guidelines. No new references added.
08/01/2024	Document updated with literature review. The following changes were made in Coverage: 1) Changed "OR" to "AND" in the Phlebectomy section: 2b criteria now states "Class 4, 4a, 4b, 4c, 5, 6, or 6r on the CEAP Clinical Findings table. (Photos may be required); AND" 2) Updated the term patient(s) to individual(s) throughout coverage; intent unchanged. Added references 51, 53, 74; others updated.
3/15/2024	Document updated with literature review. The following changes were made in Coverage: 1) Endovascular section: a) modified vein size criteria to include "throughout the length of vein to be treated"; b) added to the reflux criteria (2d) "throughout the segment to be treated (reflux in the saphenofemoral junction alone does not qualify for treatment); c) modified Note 4 under Treatment Session Limits: Replaced "one or both legs" verbiage with "each" for a maximum of five sessions per leg during a period of 12 months. Added "(Great saphenous vein [GSV], Small saphenous vein [SSV], anterior accessory great saphenous vein [AAGSV], posterior accessory great saphenous vein [PAGSV], perforators)". Clarified that requests beyond the initial session limits require evidence of ablation failure. 2) Phlebectomy section: a) removed 3 mm vein size requirement; b) added 2c "there is no incompetence in the saphenous veins. This requirement does not have to be met if phlebectomy is performed concurrently with an ablation of a saphenous vein"; c) revised treatment session limit verbiage under Note 5 to state "Requests for treatment extending beyond the initial session limits during a 12-month period will be subject to a new medical necessity review, including submission of all materials normally required for an initial review". 3) Sclerotherapy section: a) removed "and/or perforator veins" from the existing medically necessary statement; b) modified duplex doppler criteria to "no saphenous incompetence in the area to be treated" c) removed "requested or" from exception #4; d) Note 6: defined truncal veins "(i.e., great saphenous vein [GSV], anterior accessory saphenous vein [AASV], posterior accessory saphenous vein [PASV]"; e) Note 7 modifications: i.) revised language regarding treatment within 12 months of the initial varicose vein procedure and removed bullet/language for treatment sessions

	extending beyond the initial 12 months; ii.) modified from "saphenous ~~veins and~~ tributaries" to state "saphenous tributaries" iii) removed "without additional clinical documentation. For sclerotherapy of perforator veins, a maximum of two sessions per leg is allowable in a 12-month time period beyond the three allowable sessions for standard sclerotherapy of the saphenous veins and tributaries". Added references 20. 33, 55, 62 71, 76; others updated, some removed.
01/01/2023	Document updated with literature review. The following changes were made to Coverage: 1) Section I: Endovascular and Open Vein Procedures: a) modified language to exclude use of cyanoacrylate (VenaSeal) on perforators; and b) modified language to exclude use of truncal ablation with stabilized microfoam (Varithena) on small saphenous veins (SSV) and/or perforators. c) expanded note 4 to state "If an ablation (such as RFA or EVLA) is performed on a truncal vein, then a second procedure (such as VenaSeal or Varithena) may not be performed on the same truncal vein within a 12-month period." 2) Updated CEAP classification table in each section within coverage to include "C4 changes in skin and subcutaneous tissue secondary to chronic venous disease". Added references 2, 3, 20, 29, 60, 66, 72; others updated, some removed.
04/01/2022	The following change was made in Coverage: Removed the term "persistent" in relation to vein size from the following lines/sections below: Line 43 in section I Endovascular and Open Vein Px, Line 95 from Section II Phlebectomy (1a), and Lines 118 (2a), 139 (2c), 182 (2c) from Section III Sclerotherapy. Added "equal to" to vein size on line 82 (NOTE 6).
01/01/2022	Document updated with literature review. The following change was made to Coverage: Updated CEAP classification table in each section within Coverage to include C2r recurrent varicose veins and C4c Corona phlebectatica. Added references 34, 63: others updated, some removed.
05/01/2021	Document updated with literature review. All sections within Coverage were significantly revised. Added references 4, 31, 37-39, 45, 60, 63, 65; others updated, some removed.
09/01/2019	Document updated with literature review. Significant changes were made in Coverage: 1) Section I: Endovascular and open vein procedures: a) Added duplicate greater saphenous vein; b) added pain as a symptoms of varicose vein insufficiency 2) Section II: Phlebectomy a) Added CEAP classification table; 3) Section III: Sclerotherapy: a) Expanded doppler requirements to include size requirement equal to or greater than 3 mm and reflux more than 500 ms; b) Expanded Note to state "the patient has previously met the above criteria for sclerotherapy of the greater saphenous vein (GSV), small saphenous vein (SSV), GSV/SSV accessory veins, perforator veins and saphenous tributaries; c) Removed standing photograph requirement from Note 2; d) Added experimental, investigational and/or unproven for sclerotherapy of isolated tributary and/or perforator veins; 4) a) Added

	Section IV: New section for Non-Thermal Non-Tumescent Techniques which changed cyanoacrylate adhesive (e.g., VenaSeal®) from EIU to conditionally covered when criteria is met; b) Added NOTE #3: Treatment session limits; 5) Section V: Other: a) Added endovenous catheter directed chemical ablation with balloon isolation as experimental, investigational and/or unproven; b) Removed cyanoacrylate adhesive as experimental, investigational and/or unproven 6) Removed "Grade II or higher" requirement for compression stockings. 7) Expanded the duplex criteria in each section (I-IV) to be performed within 12 months, added reverse Trendelenburg position, document requirements including specific vein, vein size, and classification/location of vein to be treated. Added references 1-10, 19, 22, 26, 28, 29, 31-33, 35-38, 40, 41, 43, 44, 68, 69. Some references removed.
07/01/2017	Document updated with literature review. The following changes were made to Coverage: 1) CEAP classification was subdivided into 2 separate classes: C4a Pigmentation and eczema; C4b Lipodermatosclerosis and atrophie blanche 2) Added note to refer to SUR701.015 for Therapeutic Embolization and Vessel Occlusion 3) Removed Transcatheter occlusion or embolization for treatment of varicose veins is considered experimental, investigational and/or unproven as there is coverage in place under policy SUR701.015 Therapeutic Embolization and Vessel Occlusion.
08/15/2015	Document updated with literature review. The following was added to Coverage: Treatment of varicose veins with VenaSeal® is considered experimental, investigational and/or unproven.
04/15/2015	Document updated with literature review. The following changes were made to Coverage: 1) The criteria for Sclerotherapy was completely moved from Section I to Section III Sclerotherapy; 2) Notes 1, 2 and 3 (in Section I) were combined into NOTE #1: Treatment Session Limits; 3) Notes 4, 5 and 6 (in Section III) were combined into NOTE #2: Treatment Session Limits; 4) Exception #5 under Sclerotherapy was renumbered from Exception #4, and was revised to be "* EXCEPTION #5: If sclerotherapy was requested or performed at the time of initial endovascular or open procedure(s), no further documentation is needed."; 5) The bullet, "e) Endovascular sclerotherapy" was removed from the list of procedures under Section I ENDOVASCULAR AND OPEN VEIN PROCEDURES; 6) The following was added to Coverage: Mechanochemical ablation of any vein is considered experimental, investigational and unproven, including but not limited to ClariVein® Infusion System.
01/01/2013	Document updated with literature review. The following were removed from Coverage: 1) Following ERFA or ELA there must be an observation period of at least six weeks prior to any other surgical intervention; 2) Radiologic or ultrasonic guidance of needle placement, when used to introduce a catheter, probe or sclerosant into the vein, is considered integral to the procedure being performed; 3) Puncture aspiration of abscess, hematoma, bulla or cyst, when used to aspirate a blood clot from a previously sclerosed vein before

	performing another ablative procedure, is considered integral to the procedure being performed. The following were added to Coverage: 1) Criteria for all treatments was revised to state the patient is symptomatic with one or more of the symptoms of varicose vein insufficiency; 2) Endovenous cryoablation of any vein is considered experimental, investigational and unproven. 3) In Coverage, the following Notes were added: Note # 1— These procedures are limited to one session for the greater saphenous vein of one or both legs and one session for the lesser saphenous vein of one or both legs, and one session for the perforator veins of one or both legs for a maximum of three sessions per leg, during a period of 12 months; Note #2— Requests for treatment extending beyond the session limits per leg during a 12 month period will be subject to a new medical necessity review, including submission of all materials normally required for an initial review; Note #3— Requests for treatment sessions extending beyond 12 months from the initial invasive treatment session will be similarly subject to a new medical necessity review, including submission of all materials normally required for an initial review; Note # 4—Coverage for sclerotherapy is limited to a maximum of three sclerotherapy treatment sessions per leg, without additional clinical documentation, when performed within 12 months of the initial invasive varicose vein procedure; Note # 5—Requests for additional sclerotherapy treatment, extending beyond the maximum three treatment sessions per leg, may be considered for coverage when stated criteria have been met; Note # 6—Requests for treatment sessions extending beyond one year from the initial invasive treatment session will be similarly subject to a new medical necessity review, including submission of all materials normally required for an initial review.
08/01/2010	Revised and updated policy. The following changes were made: (1) removed color from "duplex Doppler color and/or spectral flow ultrasound study". (2) removed requirement that ultrasound study be done without the Valsalva maneuver. (3) added six week waiting period for conservative therapy for CEAP Class 2 or 3. (4) added six week observation period between ERFA/ELA and any other surgical procedure on the same leg, for CEAP Class 2 or 3. (5) added a statement that surgical treatment for CEAP Class 1 is cosmetic.
12/15/2009	Revised and updated policy. The following changes were made: (1) removed four month waiting period for conservative therapy. (2) removed four month observation period between ERFA/ELA and any other surgical procedure. (3) added spectral to "duplex Doppler color and/or spectral flow ultrasound study".
05/15/2009	Revised/Updated Entire Document
05/15/2008	Coverage Revised
02/01/2008	Revised/Updated Entire Document
09/01/2007	Coverage Revised
08/01/2007	Codes Revised/Added/Deleted. Coverage Revised

05/15/2007	Coverage Revised
01/01/2007	Revised/Updated Entire Document
08/01/2006	Coverage Revised. Revised/Updated Entire Document
01/01/2006	Coverage Revised
04/01/2004	Codes Revised/Added/Deleted
01/01/2004	Revised/Updated Entire Document
11/01/2000	Revised/Updated Entire Document
11/01/1999	Revised/Updated Entire Document
09/01/1996	New Medical Document