Medical Coverage Policy

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Varicose Vein Treatments

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Related Coverage Resources

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health

benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses varicose vein treatment. Varicose veins result from weakening or incompetence of a one-way valve, leading to reflux (i.e., reverse flow) of blood in the vessel. Methods of treatment that been investigated and proven effective for the treatment of varicose veins include ambulatory phlebectomy, ligation and excision, radiofrequency ablation (RFA), endovenous laser therapy (EVLT), endovascular embolization with cyanoacrylate adhesive, and sclerotherapy.

Coverage Policy

Coverage for treatment of varicose veins varies across plans. Refer to the customer's benefit plan document for coverage details.

If coverage is available for the treatment of varicose veins, the following conditions of coverage apply.

MEDICAL NECESSITY CRITERIA FOR HIGH RISK INDICATIONS

Ambulatory phlebectomy, ligation and excision, RFA (radiofrequency ablation), EVLT (endovenous laser therapy), endovascular embolization with cyanoacrylate adhesive (e.g.,VenaSeal™ Closure System) and/or sclerotherapy* (i.e., liquid, foam, ultrasound-guided, endovenous chemical ablation, endovenous microfoam) is considered medically necessary for ANY of the following HIGH RISK varicose vein indications:

- leg ulceration(s) due to saphenous vein insufficiency refractory to conservative management
- recurrent bleeding from the saphenous vein or other varicosity
- history of a significant episode of bleeding from a varicosity

*** Note: Sclerotherapy using a sclerosant approved by the U.S. Food and Drug Administration for the intended use.**

MEDICAL NECESSITY CRITERIA FOR LOWER RISK INDICATIONS

Ligation and excision, endovascular embolization with cyanoacrylate adhesive (e.g.,VenaSeal™ Closure System), RFA and/ or EVLT for the treatment of symptomatic saphenous varicose veins is considered medically necessary for ANY of the following indications:

- pain resulting in a clinically significant functional impairment (e.g., inability to perform household chores or prolonged standing, interference with essential job functions)
- recurrent phlebitis or thrombophlebitis
- refractory dependent edema
- persistent stasis dermatitis
- chronic cellulitis

when ALL of the following criteria are met:

- a Duplex ultrasonography evaluation and report, performed no more than 12 months prior to the requested procedure, confirms incompetence/reflux (duration of retrograde or reverse flow ≥ 0.5 seconds) and documents vein size ≥ 3 mm
- documentation of **BOTH** of the following:
  - previous invasive treatment(s) of varicose veins (if any)
  - failure or intolerance of medically supervised conservative management, including but not limited to compression stocking therapy for three consecutive months
- a clearly defined treatment plan including the procedure (CPT®) codes for the planned interventions, and whether the proposed treatment is to the left leg, the right leg, or both legs

Adjunctive ambulatory phlebectomy or primary (i.e., initial) sclerotherapy* (liquid, foam, ultrasound-guided, or endovenous chemical ablation, endovenous microfoam) is considered medically necessary treatment of symptomatic varicose veins or tributaries greater than or equal to 3 mm when reflux proximal to the incompetence (i.e., at the saphenofemoral or saphenopopliteal junction) is concurrently being or has previously been treated (i.e., ligation and excision, RFA, and/or EVLT).

***Note: Primary (i.e., initial) sclerotherapy for these indications, using a sclerosant approved by the U.S. Food and Drug Administration for the intended use, is limited to a maximum of three (3) sclerotherapy treatment sessions per leg.**

MEDICAL NECESSITY CRITERIA FOR SECONDARY SCLEROTHERAPY TREATMENT SESSIONS (i.e., RETREATMENT, SUBSEQUENT TREATMENTS)
One or more series of three (3) secondary sclerotherapy treatment sessions (i.e., retreatment, subsequent treatments) is considered medically necessary when ALL of the following criteria are met, for each series being requested:

- symptomatic varicosities ≥ 3mm persist or have recurred following a previously completed series of primary or secondary sclerotherapy
- inadequate clinical response to a recent trial of medical management including leg elevation and compression
- absence of reflux proximal to the incompetence (i.e., at the saphenofemoral or saphenopopliteal junction)
- submission of a clearly defined treatment plan including the procedure codes requested as well as the number of treatment /procedures clinically indicated

NOT MEDICALLY NECESSARY/EXPERIMENTAL/INVESTIGATIONAL/UNPROVEN
The following varicose vein treatments are each considered cosmetic in nature and not medically necessary:

- treatment of telangiectasis or varicose veins that are less than 3 mm in diameter by any method
- sclerotherapy with glycerin/glycerol
- intense pulsed-light source (photothermal sclerosis) treatment of a varicose vein

The following varicose vein treatments are each considered experimental, investigational or unproven (this list may not be all-inclusive):

- non-compressive sclerotherapy
- transdermal laser therapy
- transilluminated powered phlebectomy (TIPP, TriVex™)
- sclerotherapy (i.e., liquid, foam, ultra-sound guided, endovenous chemical ablation, endovenous microfoam) when performed for ANY of the following indications:
    - sole treatment of accessory, reticular or varicose tributaries without associated occlusion of the saphenofemoral or saphenopopliteal junction
    - incompetence that is isolated to the perforator veins
- as a sole (i.e., standalone) treatment for reflux occurring at the saphenofemoral, saphenopopliteal junction or of the great saphenous vein (GSV)
- endomechanical ablative approaches using rotating catheter (e.g., ClariVein™ Catheter) (e.g., mechanical occlusion chemically assisted ablation [MOCA], mechanic-chemical endovenous ablation [MCEA], mechanically enhanced endovenous chemical ablation [MEECA)
- endovenous catheter directed chemical ablation with balloon isolation
- coil embolization
- cryostripping (including cryoablation, cryofreezing, transilluminated cryosurgery) of any vein
- external valvuloplasty
- ambulatory selective varicose vein ablation under local anesthetic (ASVAL)

General Background

Varicose veins are swollen bulging veins that lie just below the surface of the skin, usually occur in the legs, and most commonly result from chronic venous insufficiency. The venous system of the lower extremities is separated into two main systems: the deep venous and the superficial venous system. The two systems are connected by perforator veins. The deep venous system comprises the popliteal and femoral veins; the superficial venous system comprises the great saphenous (GSV) and small saphenous (SSV) veins. The GSV generally measures 3–4 mm in diameter in the upper thigh; the GSV meets the femoral vein at the saphenofemoral junction (SFJ). The SSV is not usually larger than 3 mm in diameter and connects with the deep veins at the saphenopopliteal junction (SPJ) in the knee area. The accessory saphenous vein (ASV) arises from the GSV and is considered a GSV tributary. Anatomically the ASV originates at the distal thigh, courses upwards outside the saphenous compartment parallel to the GSV, and drains into the femoral vein, GSV or tributary above or below the SFJ. Perforator veins are veins of the lower extremity that drain from the superficial veins to the deep veins. Varicose tributaries are veins that empty into a larger vein.

GSV reflux is the most common source of chronic venous insufficiency in up to 70% of individuals, followed by the SSV in 18- 20% and AASV lest commonly, in 10%. Incompetence of the superficial venous system typically results from failure of valves at the SFJ and the SPJ with resulting pressure that is worse at the more distal area of the vein. Incompetence of the perforating veins also leads to increased pressure in the superficial venous system due to the pump mechanism of the calf.

Varicose veins vary in size from 3–10 mm, on average. Symptoms that have been associated with varicose veins of the lower extremities result from inadequate emptying of the vein (i.e., venous insufficiency) and include pain, cramping, aching, burning, throbbing, swelling and the feeling of heaviness or fatigue in the leg. Saphenous varicose veins can ultimately result in intractable ulcerations and recurrent bleeding. Patients with larger varicosities (e.g., varicose veins greater than 3 mm in diameter) are more prone to thrombophlebitis and other complications than those with smaller varicosities. Chronic cellulitis may also be associated with varicosities.

Telangiectases are permanently dilated blood vessels, also called spider veins that create fine red or blue lines on the skin. They are similar to varicose veins but are limited to the dermis and are not usually more than 3 mm in diameter. They are not typically associated with symptoms, and treatment is generally considered cosmetic in nature and not medically necessary.

In some women varicose veins develop during pregnancy. However, treatment for those resulting from pregnancy is not medically necessary as most varicosities will spontaneously resolve within 4–6 months after delivery. In nonpregnant women vulvovaginal varicosities may be associated with varices of the lower extremity. They are often asymptomatic although when symptoms occur and conservative measures fail, invasive treatment options may include sclerotherapy and /or stab phlebectomy, similar to lower limb varicose vein treatments. If there is evidence of venous insufficiency in the lower extremities sclerotherapy or stab phlebectomy may be performed as adjunctive treatment for vulvar varices (Johnson, 2019).

Varicose veins of the upper extremity are rare and there are few reports in the published, peer-reviewed medical literature dealing with the management of upper extremity varicosities (Welch and Villavicencio, 1994; Duffy, et al., 1999; Lee, 2002; Bowes and Goldman, 2002). However, authors have reported successful outcomes utilizing methods of treatment similar to lower extremity varicosities (e.g., sclerotherapy, ligation and stripping, phlebectomy).

Disparity in varicose vein disease and treatment has been evaluated in the medical literature. Pappas recently published a retrospective chart review of prospectively collected data analyzing a cohort of 66,621 patients with chronic venous insufficiency across 78 centres in the USA to study treatment outcomes according to race. Of the total cohort, 17% were African American, 3% were Asian, 18% Hispanic, 55% White and 8% Other. Pappas noted that prevalence was similar between African Americans and Hispanics, Asians presented as the lowest group while the highest prevalence was found for people who self-identified as White. A vast majority of disease was seen in women across all patient race groups, with the exception of Hispanic patients who were more often male with a 5:1 ratio. Hispanics required the fewest procedures and demonstrated the best outcomes after treatment. African Americans required the largest number of treatments to achieve results similar to other races. The authors also found that the incidence of chronic venous disease increases with age only in Whites (Pappas, et al., 2020). Another author group, Chan and colleagues (2021), evaluated varicose vein treatment specifically in Asian individuals from Singapore and Asia. They too noted chronic venous insufficiency is less prevalent in the Asian population and lower than non Hispanic whites although the authors stated they expect this to increase due to increased obesity and aging. Some studies have shown Asians present at a younger age and with less severe symptoms. Anatomically, Asians have smaller truncal saphenous veins, and longer segments of reflux compared with Caucasians. Of note, VenaSeal is indicated in Caucasians with GSV diameter > 5mm, however the median diameter of the GSV in Asian subjects is 2.9 mm, so in the author's opinion many individuals would be undertreated. Furthermoe, due to the longer area of reflux in Asians, VenaSeal is more advantageous and can reach further than procedures such as endovenous laser, along with less potential for nerve injury and skin damage. Asians also have veins which lie more superficially (N3 veins) related to lower body mass index scores and radiofrequency ablation may result in a higher number of thermal skin injuries in Asian individuals. Some authors reported modifying treatment protocols, for example in Asian populations, have resulted in clinical outcomes that are comparable to those of Western/European studies.

DIAGNOSIS AND CLASSIFICATION

Various ultrasound technologies are used in conjunction with other noninvasive testing to determine the physiological characteristics of the varicosities, as physical exam alone may not be reliable. Duplex ultrasound, Doppler ultrasound and plethysmography may all be used to diagnose

varicose veins. Duplex ultrasound of the lower extremities for evaluation of reflux should be performed in the upright position, unless the patient is unable to stand; eliciting reflux by distal compression and release is most appropriate (Matsuda, et al., 2020). In most cases, once the initial vein mapping is performed, it is not essential that follow-up scanning be done for subsequent treatment sessions. It has not been demonstrated in the published medical literature that repeat Duplex or Doppler studies are essential for the successful outcome of the procedure when performed as part of a series of sclerotherapy sessions. Also, routine use of any of these tools in the absence of venous symptoms or clinical evidence of venous insufficiency or reflux is not considered a medical necessity. Photographs or diagrams are often helpful in assessing the size and extent of the varicosities.

The CEAP classification is a method commonly used to document the severity of chronic venous disease and is based on clinical presentation (C), etiology (E), anatomy (A), and pathophysiology (P) (See Table 1). Each classification can be further defined as follows (Lurie, et al., 2020) (See Table 1):

Table 1: CEAP Classification

Class	Definition
C - Clinical Classification	**C0** No visible or palpable signs of venous disease **C1** Telangiectases or reticular veins **C2** Varicose veins **C2r** Recurrent varicose veins **C3** Edema **C4** Change in skin and subcutaneous tissue secondary to CVD **C4a** Pigmentation and/or eczema **C4b** Lipodermatosclerosis and/or atrophie blanche **C4c** Corona phlebectatica **C5** Healed venous ulcer **C6** Active venous ulcer **C6r** Recurrent active venous ulcer **CS** Symptoms, including ache, pain, tightness, skin irritation, heaviness, muscle cramps, as well as other complaints attributable to venous dysfunction **CA:** Asymptomatic
E - Etiology	**Ep** Primary **Es** Secondary **Esi** Secondary intravenous **Ese** Secondary extravenous **Ec** Congenital **En** No cause identified
A - Anatomy	**As** Superficial veins **Ap** Perforator veins **Ad** Deep veins **An** No venous location identified
P - Pathophysiology	**Pr** Reflux **Po** Obstruction **Pr.o** Reflux and obstruction **Pn** No venous pathophysiology identified

Classification of disease starts with an initial assessment and is often not entirely completed until after surgery and histopathologic assessment. As a result, it is recommended that CEAP

classification value be followed by the date of examination. Venous disease can be reclassified at any given time. It is also recommended that the level of investigation be included, with Level I representing the office visit, Level II representing noninvasive venous laboratory testing, and Level III representing invasive assessment and more complex imaging studies.

The Venous Clinical Severity Score (VCSS) is an assessment tool used to complement the CEAP scoring system of varicose veins. This tool uses both physician determined and patient reported elements, which include ten parameters graded from zero to three depending on severity (pain, varicose veins, venous edema, pigmentation, inflammation, induration, number of active ulcers, duration of active ulcers, size of active ulcers, and compliance with compression therapy) to establish a baseline against which to compare progression over time and/or effects of intervention (Moneta, et al., 2021).

TREATMENT

Conservative medical practices that may be used in the management of varicose veins include leg elevation, analgesia for symptom relief and avoidance of prolonged periods of standing. Compression therapy, the use of custom-fit compression stockings with pressure gradients, a mainstay of initial/conservative management, is routinely attempted prior to stripping, ligation, sclerotherapy or other, more invasive procedures. The amount of compression required for treatment of stasis dermatitis or ulceration is between 35 and 40 mm Hg, for varicose veins, for mild edema and leg fatigue the recommended pressure is 20 to 30 mm Hg (Habif, 2009). When conservative measures fail, treatment options rely on identifying and correcting the site of reflux and on redirecting the flow of blood through veins with properly functioning valves. No single method of treatment is universally employed in the literature; the intervention selected is generally dependent upon the competency of deep and perforating veins, and the site and degree of reflux. Surgery is commonly used to treat mainstem varicose veins. Endovenous thermal ablation procedures, which include radiofrequency ablation (RFA) and endovenous laser therapy (EVLT) are often performed as initial treatment. Sclerotherapy treatment performed on the same day as a primary treatment or a different day as an adjunct treatment of tributary veins may be required for an unsuccessful vein occlusion.

An initial treatment may be referred to as primary treatment and secondary treatment may be referred to as retreatment. Many patients require a combination of techniques (ablation, phlebectomy, sclerotherapy) to correct symptoms associated with venous insufficiency, most of which can be performed in a single treatment session. Staging of ablative varicose vein treatments on different days is rarely clinically appropriate. During an initial treatment session, only one primary thermal ablative procedure may be requested for the initial vein treated and one add-on procedure may be requested per extremity for any subsequent vein(s) treated. Guidelines from the American Venous Forum, the Society for Vascular Surgery, the American Vein and Lymphatic Society, and the Society of Interventional Radiology indicate that the mean number of saphenous vein ablations per person ranges from 1.3 to 1.9 (Masuda, et al., 2020). Treatment involving three or more ablative procedures per extremity is infrequent however may be necessary in the presence of advanced venous insufficiency.

Complications associated with varicose vein treatment vary and are dependent on the type of treatment employed. Complications that may result from sclerotherapy and phlebectomy include but are not limited to hyperpigmentation, allergic skin reactions, migraine-like symptoms (particularly from foam sclerosants), pain at the injection site, superficial and deep thromboembolic events and subcutaneous hematomas. Most complications are transient and resolve with conservative measures. Subcutaneous hematoma formation is easily managed with warm compresses and nonsteroidal anti-inflammatory medications. Thromboembolic events although rare can be life-threatening and may require anticoagulation (Lew, Weaver, 2015; Alaiti,

2021). Complications associated with thermal ablation techniques are usually minor and self-limiting; serious events are rare.

Invasive Approaches

Sclerotherapy: Sclerotherapy is an invasive procedure used to eradicate small to medium sized varicose veins of the superficial venous system (great and small saphenous veins). When reflux is present at the junction, sclerotherapy should be performed in addition to surgical ligation and division of the junction, promoting control of the point of reflux. Injection of the vein at its junction and of the incompetent perforating veins has been proposed as an alternative to ligation; however, the scientific literature does not firmly support the efficacy of this procedure. Sclerotherapy has not been shown to be effective as a sole treatment of larger incompetent veins and is often used with other approaches to treat significant varicosities. Vahaaho and colleagues (2018) completed five year follow-up for subjects with GSV reflux (5-10 mm in diameter) who were randomized to undergo ultrasound guided foam sclerotherapy (UGFS) (n=76), endovenous laser ablation (EVLA) (n=73) or open stripping with phlebectomy (n=65). At five years post treatment 77.6% of subjects were available for follow-up, UGFS had inferior occlusion rates in comparison to EVLA and open surgery (51%, 89% and 96% respectively); the difference between UGFS and the EVLA or surgery group was statistically significant ($p< 0.001$). While a majority of varicosities are related to valvular incompetence (reflux) of the great or small saphenous veins, some individuals may develop symptoms despite the absence of underlying reflux. Sclerotherapy as a sole therapy has been proposed for these individuals however the evidence base supporting this use is not robust (Corabian, et al., 2004). There is a paucity of evidence to support the clinical effectiveness of sclerotherapy in the absence of incompetence at the saphenofemoral or saphenopopliteal junction, overall effectiveness is dependent on the size, location, number of varicosities involved, and patency of the deeper veins below (Perrin, et al., 2011; Alguire, Scovell, 2020).

Echosclerotherapy is a type of sclerotherapy using liquid or foam sclerosant, also referred to as ultrasound-guided sclerotherapy, or endovenous chemical ablation (ECA), which employs real-time ultrasound during the sclerotherapy procedure to help locate deep or inaccessible sites. Echosclerotherapy is indicated for treatment of veins below the surface, such as deep veins and other varices that are difficult to visualize. The Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society (Gloviczki, et al., 2023) and the European Society of Vascular Surgery (2022) recommend symptomatic tributary veins be treated by ultrasound-guided liquid sclerotherapy or foam chemical ablation.

Foam sclerotherapy, which involves the use of a sclerosing solution that has been forcibly mixed with air or gas (e.g., carbon dioxide) to create a foam agent, is often used in large-diameter vessels and with the use of ultrasound. Ultrasound is used to monitor the foam distribution. Foam sclerosant forces blood out of the vein and allows for less dilution of the sclerosant and more contact with the endothelium (Lew, Weaver, 2015). Overall, authors generally agree foam sclerotherapy is a safe and effective method of treating varicose veins (Rabe, et al., 2004; Wright, et al., 2006; Kendler, et al., 2007; Uurto, et al., 2007; Subramonia and Lees, 2007; Jia, et al., 2007; Darvall, et al., 2009). In addition, this method is supported by professional societies and organizations as being safe and at least equally if not more effective than liquid sclerotherapy (Society for Vascular Surgery/ American Venous Forum [Glovicki, et al., 2011]; European Guideline Conference 2012 [Rabe, et al., 2013], European Society for Vascular Surgery, 2022). As with sclerotherapy in general, the need for repeat treatment sessions when using ultrasound or foam methods has been reported in the literature.

Although echosclerotherapy has been investigated as an alternative to traditional saphenous vein ligation and stripping (Min, Navarro, 2000; Bountouroglou, et al., 2006), there is insufficient evidence in the medical literature to support safety, efficacy and improvement in long-term clinical

outcomes when used for this indication. Evidence consists mainly of case series with few comparative trials and mixed reported clinical outcomes. The American College of Phebology guidelines for treatment of refluxing accessory saphenous veins support use of ultrasound guided sclerotherapy for treatment of symptomatic incompetence of the accessory great saphenous veins (strength of recommendation Grade I [strong], Level of Evidence C [low]) (Gibson, et al 2017).

There is no consensus in the published scientific literature regarding the optimal number of sclerotherapy treatments required to reduce the symptoms associated with varicose veins and the number of treatments needed to resolve symptoms varies among patients. Sclerotherapy is the treatment of choice for varicose veins that are 2–4 mm in diameter; large areas of veins can usually be eradicated using two to three treatment sessions. Vessels 4–6 mm in diameter may be treated by sclerotherapy or ambulatory phlebectomy.

The primary aims of sclerotherapy are to prevent complications of varicose disease and relieve symptoms; cosmetic improvement in the leg's appearance is an added benefit. Treatment provided solely for cosmetic purposes is not considered a medical necessity.

In compressive sclerotherapy, the most commonly performed method of sclerotherapy, compressive dressings are applied after injection of the sclerosing agent, while the limb is elevated and the vein is drained. External compression and internal decompression (e.g., walking) stimulates fibrosis, which contributes to obliteration of the entire vein wall. Non-compressive sclerotherapy involves injecting a sclerosant into the non-elevated (blood-filled) vein without applying a compressive dressing. This method of therapy has not been shown to be effective in producing long-term obliteration of the incompetent veins.

Various sclerosing agents have been approved by the U.S. Food and Drug Administration (FDA) to treat varicose veins of the lower extremities. Two most commonly used include sodium tetradecyl sulfate (Sotradecol®) and polidocanol (Asclera®); polidocanol was approved by the FDA March 2010 for the treatment of small spider veins and reticular veins. According to the manufacturer Asclera has not been studied in varicose veins larger than 3mm. Other agents such as morrhuate sodium (Scleromate™ morrhuate sodium) although FDA approved are not used as commonly. Glycerin/ glycerol is an osmotic dehydrating agent which is primarily used for the treatment of residual telangiectasias (Duffy, 2010). Nonetheless, there is no evidence-based consensus on the optimal type, dosage or concentration of the sclerosing agent.

Transilluminated sclerotherapy is a procedure that employs the use of a hand-held vein light (e.g., fiberoptic illuminator) to assist with identification of varicose veins. When placed on the skin the illumination devices theoretically allow visualization of deeper veins, that often serve as feeder veins, for which sclerotherapy can then be performed. Nevertheless, the use of illumination and other similar devices is considered integral to the sclerotherapy procedure.

Endovenous Microfoam (e.g., Varithena™): Varithena™ (polidocanol injectable foam) (Biocompatibles UK, Ltd.; Provensis, UK) is a type of foam sclerosant referred to as "endovenous microfoam sclerosant", which is dispersed from a proprietary canister device. It is intended for intravenous injection under ultrasound guidance and is administered by way of a single cannula into the lumen of the incompetent trunk veins or by direct injection into the varicosities. According to the FDA approval "Varithena™ (polidocanol injectable foam) is a sclerosing agent indicated only for the treatment of incompetent great saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous vein system above and below the knee". Varithena has not been FDA approved for use in the SSV.

According to the manufacturer, in contrast to physician compounded foams, dispensing from the proprietary canister device allows for lower nitrogen content, a controlled density, and more

consistent bubble size minimizing the risk of gas embolic adverse events. Varithena is recommended as an alternative to sclerotherapy (liquid or foam), surgery, and other endovenous ablative methods for treating varicose veins, as either primary or adjunctive therapy. Varithena does not require tumescent anesthesia and is intended for treating incompetent greater saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous veins system above and below the knee (C2-C6). Similar to foam sclerotherapy, it is purported that ablation is achieved by foam displacement of venous blood and polidocanol-induced damage to the venous endothelium after intravenous injection into the target vein or varicosity. A thrombus forms, occludes the vein, and is eventually replaced by fibrous tissue.

Evidence in the peer-reviewed published scientific literature the supports safety and efficacy of Varithena™ for treatment of superficial venous insufficiency (Davis et al. , 2018; Kugler, Brown, 2017; Gibson et al., 2016; Vasquez, Gasperis, 2015).

Early studies compared different doses of the Varithena sclerosant with placebo (Todd, et al., 2014 [VANISH-2], Todd, et al., 2015 [VANISH-2]; King, et al., 2015 [VANISH-1]). In an ongoing five-year study, Todd et al. published the preliminary eight-week results of VANISH-2 (n=232), a pivotal trial evaluating subjects randomized to receive treatment of varicose veins with PEM 0.125% (control), PEM .5%, or PEM 1% compared to placebo injection. Outcomes were measured eight weeks following treatment using a primary endpoint measured by VVSymQ scores and secondary/tertiary outcomes, which included but were not limited to improvement in appearance, a clinically meaningful change, and response to treatment using Duplex ultrasound. The average GSV diameter was 8.7 mm; the range was a minimum of 3.1 mm and a maximum of 19.4 mm. At 8 weeks follow-up there were statistically significant improvements in VVSymQ scores and appearance for both treatment groups. Improvement in the treatment groups was also clinically meaningful, with a 64% reduction in symptoms in the pooled group compared with 22% for placebo. Duplex response (occlusion of the GSV and/or accessory veins) was achieved in 83% and 86% of subjects receiving either PEM 0.5% or 1.0% respectively. In the author's opinion GSV diameter had little effect on duplex response rates (90%, 100%, 84%, 77%, and 79% in relation to vein size <5mm, 5 to <7mm, 7 to <10 mm, 10 to <12 mm, and >12 mm, respectively). No pulmonary emboli were detected and clinically important neurologic or visual adverse events were reported. In 2015 Todd and Wright reported the one year safety and efficacy data of subjects in the initial study who received PEM 1% to assess durability of response to treatment. Primary, secondary, and tertiary outcomes were the same as the initial study. At one-year post-treatment primary and secondary measures of efficacy, using VVSymQ score, IPR-V3 and PA-V3 scores, demonstrated sustained improvements of outcomes. Additionally, both Duplex responders (occlusion) and non-responders (non-occlusion) demonstrated substantial improvements of clinical symptoms at one year (Todd, et al., 2015).

In a second pivotal trial, VANISH-1, King and colleagues (2015) published their results of a phase III, multicenter, parallel study (n=279) designed to evaluate the clinical efficacy of a single administration of ≤ 15 ml of Varithena, for reducing symptoms and improving appearance of varicose veins. The study evaluated safety and efficacy of PEM using 0.5%, 1%, and 2% compared with 0.125% (control), and placebo injection. GSV diameter at baseline averaged 7.63 mm, (range 1.5 mm to 25.9 mm), inclusion criteria did not include a restriction related to vein diameter, tortuosity or prior treatments. The primary end point was efficacy measured using a 7-day average VVSymQ Instrument score at week 8, however the study was designed to follow subjects for one and five years. Other endpoints included but were not limited to appearance, PA-V3 clinically meaningful change, Duplex ultrasound of occlusion of incompetent veins or elimination of reflux at the SF junction and change in venous clinical severity score. At eight weeks follow-up reported VVSymQ scores for pooled treatment groups and individual dose concentrations were significantly superior to placebo. Additionally mean changes from baseline to week 8 in IPR-V3 and PA-V3 scores were significantly greater for the pooled PEM than for placebo.

Duplex ultrasound response rates for the pooled and individual PEM group ranged from 59% to 83% and were superior compared to those in patients treated with 0.125% PEM. No pulmonary emboli were reported and the authors noted most adverse events were mild or moderate and resolved without sequelae.

Transdermal Light/Laser Therapy: Photothermal sclerosis, such as PhotoDerm® Vasculite™, is also referred to as intense pulsed-light source. Used as an alternative to or to complement sclerotherapy in treating small varicose veins and telangiectases (spider veins), this type of light therapy utilizes small pulses of light energy which travel through the skin, are absorbed by the blood, are then changed to heat and ultimately destroy the vein. Successful treatment requires adequate heating of the veins, and several treatments are usually required for optimal results.

Transcutaneous laser ablation, also known as transdermal laser treatment, is a type of laser therapy similar to light therapy that involves the use of a laser to treat small varicose and spider veins. Small laser pulses are delivered to the vein, causing heat, which will ultimately lead to destruction of the vein. This modality is not generally useful as a primary treatment of spider veins of the lower extremity; instead, it is employed to treat superficial vessels on the face. The treatment may result in superficial skin burns and permanent pigmentation changes.

Laser or light therapy has been indicated for the treatment of telangiectasis and cutaneous vascular lesions. However, evidence in the published scientific literature indicates that transdermal light/laser therapy has not been shown to be as effective for the lower extremities as for facial telangiectasis and smaller varicosities. The vessels in the lower extremities are located deeper and have thicker surrounding tissue. Deeper vessels require a longer wavelength and longer pulse duration to damage the vessel effectively. Additionally, because spider veins and varicosities smaller than 3 mm do not usually cause symptoms, they are considered cosmetic; hence, treatment for them is not medically necessary.

Ligation, Division and/or Excision: The traditional surgical treatment of saphenous-vein varicosities consists of surgical ligation and stripping. When the GSV and SSV have reflux or incompetence, junction ligation with or without vein stripping has been recommended; in most cases, ligation is followed by GSV stripping. During the procedure, the saphenous vein and other smaller veins are exposed through an incision in the groin, where the veins are then ligated (i.e., tied off) with sutures. A second incision is made just below the knee or at the ankle to allow access for stripping the vein. When both ends of the vein are free, a wire-like instrument is threaded through the vein, extending up to the second incision in the groin area. The vein is then pulled (i.e., stripped) and removed from the leg. Removal of the superficial symptomatic vein restores venous circulation and provides relief of symptoms. Operative excision of the vein is most often reserved for large varicosities and for those located in the medial or anterior thigh. This procedure is more invasive than thermal ablative methods and as such is perfromed less often, such as when thermal methods are contraindicated.

Cryostripping: Cryoablation uses extreme cold to cause injury to the vessel. Cryostripping of the GSV has been suggested as an alternative approach to traditional ligation and stripping. During this procedure, a cryoprobe is passed through the GSV, the probe freeze attaches to the GSV and stripping is performed by pulling back the probe. Theoretically cryosurgery requires less time, has fewer complications and results in less hospital days. Evidence evaluating cryosurgery techniques are limited in quantity and quality with mixed results (Kim, Kim, 2017**;** Lee, et al., 2015; Klem, et al., 2009; Menyhei, et al., 2008; Disselhoff, et al., 2008). Lee, et al. (2015) reported the results of a nonrandomized comparative trial evaluating cryostripping (n=32) and EVLT (n=36). Their results demonstrated similar outcomes with respect to recurrence and complication rates; three recurrences (9.4%) occurred in the cryostripping group compared with two in the EVLT group (5.6%). In one randomized clinical trial (n=494) comparing cryostripping with conventional

stripping of the GSV (Klem, et al., 2009) the authors reported that cryostripping accounted for higher failures and residual GSV and offered no benefits over conventional stripping. Menyhei et al. (2008) compared conventional stripping and cryostripping and assessed quality of life outcomes and complications (n=160) in a randomized trial. The authors reported significantly improved quality of life scores for both groups, with no difference between the two groups at six months. There was less bruising in the cryo group but no difference in post-operative pain scores between the two groups. The results of another randomized trial (n=120) indicated that EVLT and cryostripping were similarly effective at two years follow-up (recurrent incompetence 77% and 66%, for EVLT and cryostripping, respectively), however EVLT was superior with regard to duration of operation, postprocedural pain, induration and resumption of normal activity (Disselhoff, et al., 2008). Results of cryotherapy procedures for treatment of varicose veins in the published scientific literature are mixed and do not lend strong support to improved clinical outcomes when compared to more conventional methods of varicose vein treatment. Further studies are needed to demonstrate safety, efficacy, and the clinical utility of cryostripping.

Ambulatory Phlebectomy/Stab Phlebectomy: Ambulatory phlebectomy is widely accepted as an alternative to sclerotherapy, performed for the treatment of secondary branch varicose veins. It is also referred to as miniphlebectomy, hook phlebectomy or stab avulsion. In ambulatory phlebectomy, multiple small incisions are made, and the varicose veins are grasped with a small hook or hemostat. They are then clamped, divided and finally extracted. The entire varicosity can be extracted with multiple small incisions. Compression therapy has been shown to reduce bleeding and improve resorption following this method of treatment and is thus widely used for that purpose. The procedure is often performed in combination with endovenous laser ablation. Effectiveness is dependent on the type of vein treated; the results of a one systematic review (Leopardi, et al., (2010) indicated that phlebectomy appears to be a treatment of choice for smaller veins such as the lateral accessory veins, and that for larger veins such as the saphenous veins, phlebectomy may not provide the same level of success as sclerotherapy.

Transilluminated Powered Phlebectomy (TIPP): TIPP, which is similar to ambulatory phlebectomy, is another minimally invasive alternative to standard surgery for the treatment of symptomatic varicosities. Also known as the TriVex™ (Smith & Nephew Inc., Andover, MA) procedure, TIPP involves endoscopic resection and ablation of the superficial varicosity.

Subcutaneous transillumination and tumescent anesthesia help visualize and locate the varicosity, while subcutaneous vein ablation is performed using a powered resector to obliterate the vein. Tumescent anesthesia involves the infusion of large amounts of saline and lidocaine to reduce hemorrhage and of epinephrine to delay absorption of the lidocaine. During this procedure, the veins are marked with a marker, and a bright light is introduced into the leg through a small incision (2–3 cm) to enhance visualization of the veins. The power vein resector is then inserted to cut and remove the vein through suction.

Proponents of this method assert the illuminating light allows quicker and more accurate removal of the vein, leading to a more effective yet less traumatic procedure. TIPP is intended for patients who are suitable candidates for conventional ambulatory phlebectomy and may also be used as an adjunctive method to other varicose vein treatments (e.g., ligation and stripping). Eidt et al. (2021) reported the advantage of TIPP is the need for fewer incisions, however it has been associated with more postoperative pain and hematoma formation, and that cosmetic outcomes do not appear to be superior to conventional ligation/excision techniques.

The individual components of the TriVex system were approved for use by the FDA in 1999, however since that time, several other illumination and powered-resection devices have been approved and are available for use.

Evidence evaluating TIPP for the treatment of varicose veins is primarily in the form of published reviews, few comparative trials (few involving randomized groups) and both retrospective and prospective case series involving small populations and evaluating short-term outcomes (Obi, et al, 2016, Lin, et al, 2016; Kim, et al., 2012; Franz and Knapp, 2008; Passman, et al., 2007; Scavee, 2006; Chetter, et al., 2006; Aremu, et al., 2004; Shamiyeh, et al., 2003; Scavee, et al., 2003; Chesire, et al., 2002; Spitz, et al., 2000). Two controlled studies specifically compared TIPP to phlebectomy (Aremu, et al., 2004; Scavee, et al., 2003), although neither of these studies were blinded. In addition, the outcomes measured in most studies include operative time, number of incisions, complications, and cosmetic satisfaction with few patient-oriented outcomes being reported. Generally, the results of these studies demonstrate that TIPP is associated with fewer incisions (Luebke, et al., 2008; Chetter, et al., 2006; Aremu, et al., 2004; Shamiyeh, et al., 2003; Scavee, et al., 2003; Spitz, et al., 2000), comparative trials support reduction of pain following TIPP procedures (Scavee, et al., 2003; Spitz, et al., 2000) and reduced complications compared to hook phlebectomy (Spitz, et al., 2000). Operative time varies among authors and with experience. Despite reports in the published literature of a reduced number of incisions, an increase in bruising, postoperative pain and decreased quality of life during the early postoperative period has been reported in some studies. Moreover, it has been reported in the literature that technical complications may be associated with inexperience. Overall evidence in the published, peer-reviewed, scientific literature does not lead to strong conclusions that TIPP results in clinical outcomes (e.g., improved pain, less varicose vein recurrence) that are as good as treatment with standard conventional methods (i.e., hook phlebectomy). Furthermore, long-term safety and efficacy of the procedure has not been adequately demonstrated.

In 2004 NICE issued an Interventional Procedure Guidance for TIPP. The advisory committee indicated that, although the evidence suggested that the procedure is effective, the data are too limited to be conclusive and there are no long-term follow-up data (NICE, 2004a).

Endoluminal Radiofrequency Ablation (RFA): Radiofrequency ablation**,** also known as endovascular occlusion, is a treatment for symptomatic varicose veins that involves delivery of controlled radiofrequency (RF) energy through a catheter inserted into the affected vein (Society of Interventional Radiology, 2021). The heat generated by the RF energy causes the vein to contract and become occluded. The treatment is intended as a minimally-invasive alternative to standard surgery for symptomatic varicosities located mainly below the saphenofemoral or saphenopopliteal junction. RFA has also been investigated as a treatment of incompetent perforator veins (Singh and Sura, 2008; Uchino, 2007; Roth, et al. 2007; Peden and Lumsden, 2007; Gibson, et al, 2007a), however data demonstrating safety and efficacy is limited and further clinical studies are needed to support widespread use for this indication. It has been reported that recanalization rates following RFA of the perforator veins at one year follow-up was near five times the recurrence rate compared with RFA of the GSV and SSV (Aurshina, et al., 2018).

Evidence in the peer-reviewed published scientific literature supports the safety and efficacy of RFA for the treatment of symptomatic varicose veins. Most early studies were small case series with short-term follow-up (Ogawa, et al., 2005; Goldman, 2002; Weiss, 2002; Goldman, 2000), and only two included direct comparisons with standard treatments (Lurie, 2003; Rautio, 2002). RFA has been shown in a prospective nonrandomized trial to be more effective than foam sclerotherapy for closure of the GSV at one year follow-up (Gonzalez-Zeh, et al., 2008). More recently, RFA has been compared to procedures such as EVLT (Almeida, et al., 2009) and has been evaluated with and without ligation of the saphenofemoral junction (Disselhoff, et al, 2008) in randomized controlled trials. Compared to EVLT, at one month following treatment, RFA was significantly superior for measures evaluating post procedure recovery and quality of life parameters. When performed with and without ligation, at two years post procedure, there was no difference in outcomes (recurrence, degree of ablation and venous clinical severity scores) from adding the ligation procedure. The short-term results of several other studies have

demonstrated that the procedure effectively occludes incompetent veins following RFA treatment (Broe, et al., 2014; Proebstle, et al., 2011; Helmy, et al., 2011; Merchant and Pichot, 2006; Hinchliffe et al., 2006; Welch, 2006; Lurie, et al., 2005). Long-term occlusion rates were reported by Merchant and Pichot (2005). This group of authors collected data to evaluate the long-term treatment outcomes of endovascular RFA and to determine risk factors that affect treatment efficacy. In their study, the authors reported on five-year follow-up results of 1006 patients (1222 limbs) treated with radiofrequency obliteration (RFO). Immediate vein occlusion was achieved in 96.8% of limbs confirmed by Duplex ultrasound examination one week or less after the procedure. The vein occlusion rate at six months, one, two, three, four and five years was 89.2%, 87.1%, 88.2%, 83.5%, 84.9% and 87.2%, respectively. The absence of reflux rate was 91.3%, 88.2%, 88.2%, 88.0%, 86.6% and 83.8%, respectively. Over a five-year follow-up period, anatomical failure was identified in 185 limbs, 19 of which received reintervention. RFA also resulted in improved pain and less bruising compared to ligation and stripping in some studies (Hinchliffe, et al., 2006). Evidence in the peer reviewed published scientific literature supports the safety and efficacy of RFA for the treatment of symptomatic saphenous varicosities, RFA is considered an appropriate alternative to conventional procedures.

Endovenous Laser Therapy (EVLT): EVLT, also commonly referred to as endovenous laser ablation of the saphenous vein (ELAS), is a treatment alternative to surgical stripping of the greater saphenous vein. EVLT is also considered an effective treatment for the SSV (Bhayani, Lippitz, 2009) however it is not typically used for smaller veins. EVLT is performed under imaging guidance by threading a catheter through the greater saphenous vein and inserting an optical fiber through the catheter (Society of Interventional Radiology, 2021).
The optical fiber is then connected to a surgical laser, allowing high-intensity laser light to induce photocoagulation of blood and occlusion of the vein resulting from damage to the intimal wall, casuing fibrosis and obliteration of the lumen. As the catheter is withdrawn, light pulses can be repeated at regular intervals to prevent any further blood flow through the vein. The procedure is typically used to treat larger varicose veins since catheters cannot be easily passed through a tortuous vein or a vein with several turns or bends. Small, dilated branches that persist after EVLT may require additional treatments with sclerotherapy or phlebectomy (Radiological Society of North America, 2009).

Evidence in the medical literature evaluating EVLT for the treatment of saphenous vein reflux consists of both retrospective and prospective case series, published reviews, and randomized controlled clinical trials (El-Sheikha, et al., 2014; Rass, et al, 2012; Disselhoff, et al., 2011; Huisman, et al., 2009; Nijsten, et al., 2009; Kalteis, et al., 2008; Darwood, et al., 2008; Desmyttrere, et al., 2007; Sharif, et al., 2007; Gibson, et al., 2007; Rasmussen, et al., 2007; Ravi, et al., 2006; Puggioni, et al., 2006; Min, et al., 2003; Ho, 2003; Chang and Chua, 2002; Proebstle, et al., 2002; Navarro and Min, 2001). There is a large body of evidence to suggest that more minimally invasive techniques, which include both RFA and EVLT, are beneficial in the treatment of varicose veins when used alone (van den Bos, et al, 2009; Ravi et al., 2006; Sadick, 2005; Beale, et al., 2004; Teruya and Ballard, 2004; Elias and Frasier, 2004). Sample size and follow-up periods vary widely across studies; follow-up periods typically range at least one to four years on average. In some of the studies, duplex ultrasound demonstrated successful vein occlusion after initial treatment and throughout the various follow-up periods (Kalteis, et al., 2008; Gibson, et al., 2007; Desmyttrere, et al., 2007; Ravi, et al., 2006; Puggioni, et al., 2006; Min, et al., 2003). Some of the measured outcomes, such as complication rates, return to work, patient satisfaction and quality of life scores, are mixed—some authors report improvement compared to traditional surgical methods while others have not. Success rates and recurrence rates have been promising with several studies supporting clinical efficacy. Van den Bos, et al. (2009) published the results of meta-analysis demonstrating success rates of 78%, 84%, and 95% for ultrasound guided sclerotherapy, RFA and EVLT respectively, after three years. Min and associates (2003) reported a recurrence rate of less than 7% at a two-year follow-up, although

the study had a significant number of patients lost to follow-up. Nonetheless, the authors noted their results were comparable or superior to those reported for other treatment options, including surgery, ultrasound-guided sclerotherapy, and radiofrequency ablation. Puggioni et al. (2006) concluded from a retrospective review that the overall success rate of endovenous ablation techniques for occluding the incompetent greater saphenous vein was 94% at one month, although the EVLT group developed more frequent postoperative complications compared to an RFA group. Ravi et al., (2006) reported that no GSV recanalization was found at three years post EVLT and that no saphenous vein could be identified in 82.5% of limbs in their study group. Closure rates at one month, one year, two year, three year and four years follow-up were reported by Desmyttrere, et al. (2007) as follows: 98.4%, 96.8%, 97.8%, 99.3% and 97.1%, respectively. Overall, much of the evidence available suggests that endovenous closure techniques are as good as or superior to conventional ligation and stripping of the greater saphenous vein.

A multisociety consensus guideline (Kilnani, et al., 2010) states the use of endovenous ablation therapy, performed with either laser or radiofrequency devices under imaging guidance and monitoring, is an effective treatment of extremity venous reflux and varicose veins. The statement suggests that the success rate for vein GSV ablation ranges from 85-100%. The guidelines recommend using Duplex ultrasound prior to the procedure to map the necessary anatomy of the venous system, during the procedure for correct catheter placement and anesthetic delivery, and as necessary for follow-up.

Endomechanical Ablative Approach: The endomechanical ablative approach to varicose vein treatment utilizing a percutaneous infusion catheter is an emerging treatment of varicose veins. The procedure is also referred to as mechanical occlusion chemically assisted ablation (MOCA), mechanic-chemical endovenous ablation (MCEA), and mechanically enhanced endovenous chemical ablation (MEECA).The approach involves the use of a special catheter (ClariVein™ [Vascular Insights, LLC, Madison, CT]) which combines two modalities of treatment for varicose veins: endovenous mechanical vein destruction with a rotating wire and the simultaneous infusion of an FDA approved liquid sclerosant, sodium tetradecyl sulfate to enhance venous occlusion. This mechanical-chemical ablative modality (endomechanical ablative approach) is described as minimally invasive and purported to accomplish great saphenous vein occlusion without the use of tumescent anesthesia. Information available from the manufacturer of ClariVein indicates the catheter has received 510(k) clearance from the United States Food and Drug Administration (FDA) for infusion of physician-specified agents in the peripheral vasculature. Although it could not be found on the FDA site, a second device is under investigation: Flebogrif (Balton, Warsaw, Poland) and as been reported on in the medical literature. This device utilizes radial retractable cutting hooks with chemical ablation via a sclerosant foam injection (Alozai, et al, 2021).

Evidence in the published peer-reviewed scientific literature evaluating endomechanical ablation is in the form of randomized controlled trials (Mohamed, et al., 2020; Holewijn, et al., 2019; Vahaaho, et al., 2019; Lane, et al., 2016; Bootun, et al., 2014), a multicenter prospective observational report (Bishawi, et al., 2013) and retrospective or prospective observational cohorts involving small sample populations and evaluating short to mid-term outcomes (Baccelieri, et al., 2021; Mirandola, et al., 2021; Kim, et al., 2019; Mohamed, et al., 2019; Khor, et al., 2018; Tang, et al., 2016; Witte, et al., 2016; Kim, et al, 2016; Boersma, et al., 2013; Elias, Raines, 2012). Sample populations in early clinical trials ranged from 25 to 155 subjects with follow-up of six weeks to one year. More recently, authors have published results of observational clinical trials involving larger sample populations although despite occlusion rates of >90%, follow-up assessment within these trials remain limited to 6-12 weeks post-procedure (Tang, et al., 2016; Deijen, et al., 2016). One study reported three year follow-up with occlusion rates of 86.5% (Witte, et al., 2016). Clinical outcomes measured generally include occlusion rates, recanalization rates, perioperative pain, overall quality of life and general satisfaction. Compared to RFA, MOCA has been associated with a greater reduction of peri- and post-operative pain (Lane, et al., 2016;

Bootun, et al., 2014). In 2021 Ontario Health Quality reported in a technology assessment evaluating MOCA and cyanoacrylate adhesive closure that individuals whose varicose veins were treated with MOCA had poorer vein closure, but similar improvement in symptoms and quality of life as the thermal endovenous procedures. Included in their technology assessment evaluating MOCA specifically with either RFA or EVLA were a total of eight studies: four RCTs and four non RCTs.

The authors of an early clinical trial (Elias and Raines, 2012) reported a 97% total occlusion rate of the treated vein segment at 6 months post procedure (N=30). A total of 22 subjects available for follow-up at one year had total occlusion of the vein treated, and at two years 96% had total occlusion. Van Eekeren and colleagues (2013) reported the results of prospective observational study comparing RFA (N=34) and MOCA (N=34) of the greater saphenous vein. Outcome measures included RAND-36 short-form health survey, the Aberdeen Varicose Vein Questionnaire, and a 100 point VAS measured at two weeks and six weeks following surgery. Treatment time was significantly shorter in the MOCA group (P=.02). At two weeks subjects who were treated with MOCA reported significantly less postoperative pain than subjects who underwent RFA. This group also required significantly less time to resume normal activities and return to work. At six weeks there were no major complications in either group and improvement in disease specific quality of life and health status was reported for both groups. Limitations of the study included small sample size and short-term follow-up with lack of randomization.

In 2014 Bootun et al. reported the preliminary results of a RCT comparing the degree of pain subjects experienced while receiving mechanochemical ablation (n=60 legs) compared to RFA (n=59 legs). The primary outcome was perioperative pain measured by a 100-millimeter visual analog scale, with a score ranging 0-10 and return to normal activities one month post-surgery with secondary outcomes of change in quality of life and clinical scores, time to return to normal activities and work, and occlusion rates. At one month post procedures 66 % of subjects were available for follow-up. The mean maximum pain score was significantly lower in the mechanical ablation group compared to the RFA group (19.3 ± 19 mm, 34.5 ± 23 mm, respectively; [p<0.0001]). The mean time to normal activities was 3.5 ± 3.1 days in the ablated group versus 4.8 ± 4.3 days in the RFA group (*P*=0.235), and the corresponding time to return to work was a mean of 5.3 ± 8.7 days for the ablated group and 4.9 ± 3.6 days for the RFA group (*P*=0.887).The authors noted long term data, including occlusion rates at six months and quality of life scores, are yet to be determined**.**

Vun et al. (2014) reported the results of a prospective, non randomized comparative study evaluating the efficacy of ClariVein (n=55) compared to EVLT (n=40) and RFA (n=50). Measured outcomes included procedure times and pain scores using a VAS. Technical success rate was 91% for ClariVein in comparison to 93% for RFA and EVLT. Procedure time and median pain scores were significantly lower for ClariVein compared to EVLT or RFA (p<0.01). The study is limited by lack of randomization, small sample size for comparison and lack of long-term outcomes.

Kim et al. (2016) published two year clinical results of a prospective observational trial (n=126) evaluating MOCA in patients with symptomatic GSV reflux. At two years post-procedure 65 subjects were available for follow-up; 14% had adjunctive treatments consisting of either phlebectomy (9%) or sclerotherapy (5%). The authors reported 92% closure rate at 24 months post procedure, with one complete and four partial recanalizations. When compared to pre-operative values VCSS and CEAP scores improved, 63% had no residual varicose veins, and 83% were asymptomatic. Limitations of the study included small sample, lack of control group comparison, and high loss of follow-up.

Lane and associates (2016) published the outcomes of a randomized controlled trial evaluating the difference in pain during truncal ablation using MOCA (n=87) and RFA (n=83) with six months

follow-up. The proportion of subjects completing follow-up at six months were 71% (n=121). The primary outcome was measured as maximum pain and average pain experienced during truncal ablation, secondary outcomes included disease specific quality of life, general quality of life, and clinical severity scoring, return to work/normal activities, occlusion rates, and complications. Using the VAS scale maximum pain and average pain experienced during the procedure was significantly less in the MOCA group compared to the RFA group. Between groups there was no significant differences for disease specific quality of life, general quality of life, clinical severity scores, return to work/normal activities, or occlusion rates at six month follow-up. MOCA occlusion at six months was 87% versus RFA 93%. The authors acknowledged additional studies are needed involving larger populations to assess long-term outcomes**.**

Witte and colleagues (2016) published their results of a prospective case series evaluating MOCA for treatment of GSV insufficiency (n=85). Subjects were evaluated at baseline, four weeks, and one, two and three years post procedure using Duplex ultrasound, CEAP classification, Venous Clinical Severity Score (VCSS). Primary endpoints were clinical success (i.e., improvement of ≥ 1 VCSS) and anatomic success (i.e., occlusion of the treated vein); secondary outcomes were general and disease specific quality of life and re-intervention. During follow-up there were four RFA reinterventions for recanalized GSVs. Anatomic success after MOCA was 91.8% at 12 months, 89.5% at 24 months and 86.5% at 36 months. Clinical success was achieved in 83.1% of treatments. Quality of life measures showed an improvement in all time intervals compared with baseline. During the 12 to 36 month interval there was significant drop on VCSS scores, which was accompanied by a deterioration of disease specific and general quality of life. It was noted worsening of VCSS might be the result of a progression in comorbidities and may not reflect the recurrent nature of varicose veins. In the authors opinion MOCA is an effective treatment modality however clinical results decrease over time.

In 2017 Witte and associates published a systematic review evaluating MOCA as treatment of insufficient great and/or small saphenous veins. Ten unique cohort studies (1521 veins) were included in the review. The primary outcome measure was anatomical success, defined as closure of the treated vein on follow-up Duplex imaging. Secondary outcomes included technical success (i.e., ability to complete the procedure as planned), clinical success (i.e., VCSS, Aberdeen Varicose Vein Questionnaire, and quality of life), and major complications which were defined as deep venous thrombosis, pulmonary embolism or paresthesia. Outcome data was pooled, follow-up periods were clustered, and occlusion rates were evaluated. The authors noted in six of the studies there was a financial connection with the manufacturer of ClariVein. The pooled anatomical success rate after short term follow-up was 92% and at six and 12 months it was reported as 92% and 91%, respectively. Long term anatomical success rate at two and three years were 91% and 87%, respectively. Six cohorts included in the review that described VCSS showed that MOCA led to a significant improvement in quality of life scores which remained evident at 36 months, although after two years the authors noted there was a deterioration in clinical scores. In the authors opinion this may have been related to the recurrent nature of varicose veins. Major complications and nerve injury were rare (≤ 2%). (Witte, et al., 2017).

Vahaaho et al (2019) published the results of a RCT comparing MOCA (n=65) with thermal ablation, using either EVLT (n=34) or RFA (n=33), of the GSV with the primary outcome measure of occlusion rate at one year follow-up. All subjects received phlebectomy in the MOCA group but not in the RFA or EVLT group. The groups were similar in terms of age, BMI, initial GSV size, C classification, and clinical disability score. At one year 117/125 subjects were available for follow-up. At one year follow-up the treated section of the GSV was occluded in all subjects who underwent RFA or EVLT, in the MOCA group ten subjects did not have full occlusion (45/55). Larger GSV diameter in the proximal part of the GSV (8-6 mm) was associated with a higher recanalization rate. At one year post procedure quality of life scores were similar in all three groups. In 2021 the author group published three year outcomes at which time 106 (84.8%) of

subjects were available for follow-up. One patient was allowed to crossover otherwise all received the planned treatment. Occlusion rates for subjects treated with RFA or EVLT demonstrated 100% occlusion rates; the MOCA group demonstrated an 80% unassisted occlusion rate. The odds of recanalization increased as the vein diameter increased and veins with a preoperative diameter of >7 mm were more probable of recanalizing. Quality of life and clinical status improved in all treatment groups at three years (Vahaaho, et al, 2021). The authors concluded the three year occlusion rates for MOCA are inferior to RFA and EVLT. Limitations of the study included small sample population, lack of blinding and short to mid-term follow-up (Vahaaho, et al., 2021).

Despite more recent evidence, reported clinical outcomes remain short-term with mixed results. Holewijn et al. (2019) published the results of a RCT comparing MOCA (n=109) with RFA (n=104) for GSV incompetence. The primary measured outcomes included postprocedural pain two weeks post-treatment and anatomic success (i.e., occlusion) at one year. Several secondary outcomes were measured which included anatomic success, clinical success using the Venous Clinical Severity Score (VCSS), 18 to 30-day morbidity, procedural time, procedural pain, disease specific quality of life (using the Aberdeen Varicose Vein Questionnaire [AVVQ]) and general HRQoL (36-Item Short Form Health Survey [SF-36]), time to return to daily activities or work, reintervention rate, and any additional varicose vein treatment performed during 2 years of follow-up. One and two year complication rates were 86.8 and 72.4% for the MOCA group and 82.7 and 78.6% for the RFA group. The one and two year anatomic success rate was lower after MOCA (83.5% and 80.0%) compared with RFA (94.2% and 83.3%)(p=.025 and .066). There were nine complete recanalizations in the MOCA group and four in the RFA group until one year follow-up, and nine and seven complete failures, (respectively) until two years of follow-up. Absolute VCSSs were similar in both groups at one and two years follow-up, clinical success results were similar for the same timeframe (respectively: MOCA 88.75, RFA 93.2%; MOCA 93%, RFA 90.4%) and no differences in HRQoL scores were noted. In the authors opinion both techniques were associated with similar clinical outcomes at one and two years.

In 2020 Mohamed and colleagues published results of a randomized controlled trial comparing endovenous laser ablation and mechanochemical ablation using ClariVein in the management of superficial venous insufficiency. A total of 150 subjects were randomized to MOCA with 1.5% sodium tetradecyl sulfate or to EVLA, with concomitant phlebectomy as needed. The primary outcomes were intraprocedural axial ablation pain scores and anatomical occlusion at one year. The authors reported occlusion rates were lower in the MOCA group (77%) compared to the EVLA group (91%) with no significant difference between the two treatments in intraprocedural pain scores. Clinical severity and quality of life scores were not significantly different between the groups at one year follow-up. Additional follow-up is needed to evaluate the effect of recanalization on the rate of clinical recurrence.

Mirandola et al. (2021) published results of a retropsective trial involving 395 primary, symptomatic, unilateral saphenous varicose veins. A majority of the veins treated using the ClariVein catheter and polidocanol 2% liquid were GSV (92.3%), the remaining were small saphenous. Follow-up occurred at one week, one month, six months, one year and then yearly after using duplex ultrasound scans. The trial lasted five years, with a mean follow-up time of 20±18 months (range 6-60). At five years 25 subjects were available for follow-up, at which time five presented with recanalization. At two, three and four years 122, 91 and 54 subjects were available respectively. Anatomic success, defined as no recanalization longer than 5 cm, was 94% at one year, 91% at two years, 88% at three and four years, and 84% at five years. A total of 66 sbjects were lost to follow-up. Limitations include large loss to follow-up, and low number of subjects available at subsequent intervals.

Evidence in the peer-reviewed published scientific literature supporting long-term safety and efficacy of endomechanical ablative approaches to treatment of varicose veins is currently lacking.

A majority of published trials report outcomes that are less than 1-2 years on average. Randomized controlled trials comparing MOCA anatomical success to endothermal ablation are few and there is some evidence to suggest occlusion rates at three years are inferior to those of RFA or EVLT. Although evidence lends support to improved quality of life scores and clinical success in the short-term, anatomic success (occlusion rate) has been shown to deterioriate at one to three years followup. As such, additional well-designed studies are needed to support the long-term efficacy of this approach.

Other Treatments

VenaSeal: VenaSeal™ Closure System (Sapheon, Inc., Morrisville, NC) (also referred to as cyanoacrylate vein ablation [CAVA]) received FDA pre-market approval in 2015 and employs the use of cyanoacrylate embolization (CAE) and does not require tumescent anesthesia; a cyanoacrylate adhesive is injected into the vein via a catheter inserted through the skin under ultrasound, the vein is compressed, and the adhesive material changes into a solid to seal the varicose vein. Two other systems reported on in the medical literature primarily in Europe are the VariClose Vein Sealing System (Biolas, FG Group, Turkey), and VenaBlock (Invamed, Ankara, Turkey), cyanoacrylate-type adhesives, neither has been approved or cleared for marketing by the FDA.

Randomized Controlled Trials: In 2015 Morrison et al. published the early results of a randomized controlled trial evaluating CAE, using the VenaSeal Closure System (n=108) versus radiofrequency ablation (n=114) for the treatment of varicose veins. The study's primary endpoint was closure of the target vein at month 3 as assessed by duplex ultrasound. Statistical testing focused on showing non-inferiority with a 10% delta conditionally followed by superiority testing. By use of the predictive method for imputing missing data, 3-month closure rates were 99% for CAE and 96% for RFA. All primary end point analyses, which used various methods to account for the missing data rate (14%), showed evidence to support the study's non-inferiority hypothesis (all $P < .01$). Some of the analyses supported a trend toward superiority ($P = .07$) in the predictive model. Pain experienced during the procedure was mild and similar between treatment groups (2.2 and 2.4 for CAE and RFA, respectively, on a 10-point scale; $P = .11$) and there was less ecchymosis in the treated region on day 3 following CAE compared with RFA ($P < .01$). In the author's opinion, CAE was non-inferior to RFA for the treatment of incompetent GSVs at three month follow-up. The authors noted the results will be monitored for 3 years to determine long-term success rates, rates of recanalization, and chronic venous disorder (CVD) progression (Morrison, et al, 2015).

In 2017 this same group of authors published 12 month results of the study; 192 subjects were available for followup. The complete occlusion rate was similar in both groups: 97.2% in the CAE group compared with 97% in the RFA group (Morrison, et al., 2017).

In 2018 the authors published 24 month results of the VeClose trial of which 171 subjects completed; 87 from the CAE group and 84 from the RFA group. The 24 month complete closure rate was 95.3% in the CAE group compared with 94.0% in the RFA group, supporting continued non-inferiority of CAE. Symptoms and quality of life improved in both groups and there was no significant device or procedure related adverse events (Gibson, et al., 2018).

In 2019 Morrison and colleagues published 36 month follow-up of the VeClose trial with follow-up on 146 (66%) patients; 72/108 from the CAC group and 74/114 subjects from RFA group. The remaining subjects either dropped out of the study or the data could not be collected in the time period dictated by the study period. Improvement in quality of life scores were sustained in both groups, closure rates of CAE were similar to RFA (94.4%, 91.9%, respectively), although not statistically significant, and continued to support noninferiority. CAE was superior to other methods in terms of patient comfort. No significant device- or procedure-related adverse events

were reported for either group. The trial is limited by high loss to follow-up. In addition, both groups used compression stocking for seven days post treatment, use of compression stocking varied in other studies making comparisons difficult.

Morrison et al. (2020) published the five year extension results of the VeClose IDE Trial (RCT) which compared VenaSeal (n=47) to RFA (33), in addition to 9 VenaSeal roll-in subjects, for the treatment of incompetent GSV. The primary outcome of the study was complete closure of the target vein, with planned exploratory analysis of noninferiority. CEAP class, completion of the Venous Clinical Severity Score, EuroQol-Five Dimension survey, and Aberdeen Varicose Vein Questionnaire, patient satisfaction with treatment, adverse events (AEs) related to target GSV and details of adjunctive procedures were considered secondary outcomes. At 60 months, the Kaplan-Meier estimates for freedom from recanalization in the randomized VenaSeal and RFA groups were 91.4% and 85.2%, respectively, demonstrating noninferiority of VenaSeal compared with RFA. The VenaSeal group also demonstrated sustained improvements in symptoms and quality of life, lower CEAP scores, and high level satisfaction without serious adverse events during the 36 to 60 month follow-up. The authors concluded that at five years VenaSeal was safe and effective for treatment of GSV incomepetence. The primary author noted that all of his subjects had cyanoacrylate still visible at 60 months, suggesting it was a permanent implant. This study is limited by the lack of blinding as noted by the authors and the small number of subjects available at the final five year outcomes.

Joh et al. reported the results of a multicenter RCT where they compared VenaSeal with surgical stripping (N= 63 VenaSeal, 63 with SS) for incompetent GSVs. Target vein occlusion was assessed on the third day and one, three, six and 12 months postoperatively using duplex ultrasound., with the primary endpoint being complete closure of the target vein at 3 months. Pain and ecchymosis grades were evaluated as well as clinical outcomes, using venous clinical severity score (VCSS) and Aberdeen Varicose Vein Questionnaire scores. At three months complete target vein closure was observed in both groups. The postoperative pain score was significantly better in the CAC group than in the SS group (0.3 ± 0.6 in the CAC group and 1.1 ± 1.5 in the SS group; $P < .001$). The mean ecchymosis grade was 0.3 ± 0.5 in the VenaSeal group and 1.1 ± 1.1 in the SS group ($P < .001$). The venous clinical severity score and quality of life had improved equally in both groups. Adverse events after both procedures were considered primarily minor complications (9 events in VenaSeal group and 20 events in SS group). Major complications occurred in one patient who had undergone the SS procedure. At 12 months there were no recanalizations or recurrences (Joh, et al., 2021).

Observational Studies: Evidence in the form of observational case series has lent some support to safety and efficacy of endovenous cyanoacrylate embolization at 12 month follow-up (Proebstle, et al., 2015; Chan, et al., 2016; Kubach et al., 2021). Proebstle and colleagues (2015) published 12 month outcomes of a European multicenter cohort study (n=70). Subjects underwent endovenous cyanoacrylate embolization for treatment of symptomatic GSV incompetence using VenaSeal. Immediately after the procedure all but one subject had complete closure of the target GSV. The authors noted this subject also received foam sclerotherapy resulting in full occlusion. At 12 months post-procedure, 68 subjects were available for follow-up. Eight subjects developed partial recanalization during the 12 month time-frame; using life-table methods the authors reported a 12-month complete occlusion rate of 92.9%. As reported by the authors, although results are encouraging the study is limited by lack of a control group and randomized controlled trials comparing VenaSeal with endothermal ablation are still needed to establish clinical utility. Chan et al (2016) reported the results of a single center cohort of subjects who underwent endovenous cyanoacrylate embolization using VenaSeal (n=29 subjects, 59 legs). The primary outcome measure was GSV obliteration, follow-up occurred at one week, and one, six, and 12 months post procedure. The authors reported GSV closure rates were 98.2%, 94.3%, 89.7% and 78.5% respectively. At a medium follow-up of nine months no clinical recurrence of varicosity was

recorded. In addition, all subjects had improvement of SF-36 physical and mental scores, venous clinical severity scores, and Aberdeen varicose vein questionnaire scores**.**

Since 2016 additional evidence has been published evaluating cyanoacrylate adhesive (Bademci, et al., 2017; Premnath, et al., 2017; Lam, et al., 2017; Park, 2017)**,** however the evidence lacks control groups, involves short term outcomes (3-12 months), employed the use of different glues, and some populations had adjunctive varicose vein treatments using either sclerotherapy or phlebectomy, therefore strong evidence based conclusions cannot be made regarding safety and efficacy based on this evidence.

Almeida and colleagues (2017) published results of prospective trial (n=38) evaluating cyanoacrylate adhesive as treatment for saphenous vein incompetence with 36 month follow-up (Almeida, et al., 2017). Thirty eight individuals were treated with cyanoacrylate adhesive by injection of small bolus using ultrasound guidance and no anesthesia or compression stockings post procedure. Twenty nine subjects were available for follow-up at 36 months. All but two subjects had complete occlusion confirmed by duplex ultrasound (occlusion rate of 94.7%). Pain, edema, and VCSS scores improved from baseline to month 36. In the authors opinion long term occlusion rates were similar to those of other thermal and nonthermal methods. Limitations of the study include lack of a control group, high drop out rate (9/38), and small sample population.

Zierau and associates (2018) published six year outcomes from a retrospective trial using VenaSeal in 1950 veins (GSV, SSV, Accessory, Giacomini vein). A total of 1332 veins were followed over a six year period of time; 45 partial and 25 complete recanalizations were found resulting in an effectiveness closure rate of 96.4%. Post-operative nonspecific inflammatory skin reactions occurred in approximately 8% of subjects (156 treated veins) 10-14 days post-treatment, no other complications were reported**.**

Chan et al 2020 published 12 month outcomes evaluating VenaSeal for superficial reflux (37 subjects) and treatment of venous ulcers in an Asian population. The authors noted that in the Asian population the vein diameter and distribution of venous reflux are different as such the technique was modified. Follow-up occurred at 1 week, 3, 6, and 12 months post procedure. All venous ulcers were <30 cm^2 before treatment, the mean time for ulcer healing from operation was 73.6 ± 21.9 days, and the primary occlusion rate of the CVI at both 1 week and 3 months was 100%. No major adverse events were observed except for one case of deep venous thrombosis. The VCSS showed significant improvement postoperatively from 11 ± 1.63 (at baseline) to 5.6 ± 1.37 ($P < .001$) at 3-month follow-up (on a scale of 0 to 27, with the severity of symptoms at a maximal 27). The visual analog scale scores for pain were low postoperatively, decreasing from a preoperative score of 6.84 ± 1.42 to 2.72 ± 1.59 ($P < .001$) at the 3-month follow-up (on a scale of 1-10, with 10 being the most severe pain) and the median time to return to normal activities was 7 days (interquartile range, 5-7 days). The study is limited by small sample population and short term followup.

Gibson et al (2020) evaluated hypersensitivity related to VenaSeal in 286 subjects (n=379 limbs). The review combined retrospective and prospective evaluation of onset, severity [mild, moderate, severe], and duration of symptoms. The authors reported that hypersensitivity reactions occurred in 18 (6%) persons, (13 mild, 4 were moderate, 1 was severe). Second limb treatment on a subsequent day was performed in 27 patients, and no hypersensitivity reactions occurred. Symptom onset time ranged from 1 to 23 days, with a mean of 13 days (confidence interval (CI) ±3.5 days). Duration of symptoms ranged from 3 to 28 days (mean 10.8 CI ±4.9 days). The authors concluded most reactions were mild and self-limiting.

Proebstle et al. (2020) published 36 month results of a prospective multicenter nonrandomized trial evaluating treatment of GSV reflux with VenaSeal (n=70) (eSCOPE study). The primary

outcome was closure rate at six months, safety (rate of occurrence of all adverse events) was assessed at six months following the procedure, and quality of of life and clinical improvement measures were evaluated before the procedure and through a 12 month followup. Anatomic success and clinical improvement were assessed through 36 months follow-up. Complete occlusion was defined as no segments of patency exceeding 10 cm. At three years 91% of subjects (n=64) were available for follow-up with eight cases of recanalization. Closure rates (freedom from recanalization) were 91.4%, 90.0%, 88.5%, and 88.5%, at 6, 12, 24, and 36 months respectively. No serious adverse events were reported. The mean venous clinical severity score (VCSS) was statistically significant dropping to .9 from 4.3 at baseline (P< .001). In the authors opinion the three year follow-up eSCOPE study demonstrated continued anatomic and clinical effectiveness. A limitation of this study is the small sample size.

Obanion and associates (2020) published their results of a retrospective trial comparing ClosureFast RFA and adhesive closure using VenaSeal. Inclusion criteria were patients with healed CEAP 6 varicosities who had undergone closure of the truncal veins. The primary endpoint was time to wound healing Secondary outcomes included ulcer recurrence and infection rates. The median f/u was 105 days (3.5 months), there was 119 total subject (VenaSeal [n=51], RF ablation [N=68]). The authors reported that median time to wound healing after the procedure was significantly shorter for VenaSeal than for RFA (72 vs 294 days; P = .001), two RFA patients developed a postprocedure infection and the ulcer recurrence rate was 19.3% (22.1% for RFA vs 13.7% for VenaSeal; P = .25).The authors concluded that Closurefast and VenaSeal are both safe and effective treatments for truncal venous insufficiency and that VenaSeal had superior rates of wound healing compared with RF ablation for ulcers that were > $3cm^2$.

In contrast, Ay and colleagues (2021) compared traditional surgical stripping (n=62), RFA (n=70), and cyanoacrylate embolization (n=85) in terms of long-term effect on quality of life in GSV insufficiency. Outcome measures used include VCSS, 36-item Short Form Health Survey, and Chronic Venous Insufficiency quality of life questionnaire at one year post treatment. A decrease in VCSS was less pronounced in the cyanoacrylate group at one year in comparison to the two other groups (p< 0.05). The RFA group also had better improvement in the CIVIQ-14 scores than the cyanoacrylate group (p<0.05). Using the SF-36 outcome both the surgical stripping and RFA group performed better in several measures. The authors concluded that surgical stripping and RFA provided better quality of life results compared to cyanoacrylate at one year post procedure.The study is limited by small sample and short term followup.

Tang et al. (2021) reported the three month follow-up of 100 subjects who underwent treatment of GSV, SSV or AASV incompetence using VenaSeal (Singapore VenaSeal Real-World Post-Market Evaluation Study, a prospective trial). The purpose of the study was to evaluate the performance of VenaSeal closure system (VSCS) for ablating varicose veins in a prospective multicenter, multiracial Asian cohort from Singapore. The authors noted venous anatomy and truncal incompetence distribution within the leg of white patients are dissimilar to those of their Asian counterparts. As part of the study subjects were reviewed at 2 and 12 weeks for Duplex US/recanalization (defined as ≥5 cm in length), pain score, revised Venous Clinical Severity Score, EuroQol-5 Dimension questionnaire score, Aberdeen Varicose Vein Questionnaire score, 14-item Chronic Venous Insufficiency Questionnaire (CIVIQ-14) for quality of life measures, and patient satisfaction. The sample population involved participants who were of the following ethnicity: Chinese (71), Malay (11), Indian (16) and Other (2). The reported results demonstrated the following:

- Patient surveys at the 3-month interval showed high satisfaction rates, with 72 of 91 (79.1%) being extremely or very satisfied.
- By day 10, 93/100 patients (93%) resumed daily activities, whereas 36 (36%) had returned to work.

- At 2 weeks, the GSV and SSV were completely occluded in 150 of 150 (100%) and 6 of 6 (100%) veins, respectively.
- At 3 months, GSV and SSV occlusion rates were 140 of 141 (99.3%) and 6 of 6 (100%), respectively.
- Transient superficial phlebitis was reported in 27 of 151 (18 %) legs, which was self-limited, no serious adverse events were reported.
- At 3 months, revised Venous Clinical Severity Score improved from 5.00 (range, 1.00-18.00) to 1.00 (0.00-10.00; P < .001); EuroQol-5 Dimension score, from 0.686 (-0.382 to 1.00) to 1.00 (0.12-1.00; P < .001); Aberdeen Varicose Vein Questionnaire score, from 17.14 (1.29-61.15) to 4.83 (0.00-57.12; P < .001); and 14-item Chronic Venous Insufficiency Questionnaire, from 19.64 (1.79-73.21) to 7.14 (0.00-51.79; P < .001).

Meta-Analysis/Systematic Reviews: A systematic review and meta-analysis published by Shortell and colleagues (2017) evaluated MOCA and cyanoacrylate vein ablation for treatment of GSV incompetence. A total of 15 articles met the inclusion criteria and were reviewed and included seven MOCA studies (Bishwai, et al., 2014; Elias, et al., 2012; Kim, et al, 2017, Lane, et al., 2017; Ozen, et al., 2014; van Eekeren, et al., 2014; and Witte, et al., 2017) and eight CAVA studies (Almeida, et al., 2013; Almeida, et al., 2015; Bozkurt, et al., 2016; Calk, et al., 2016; Chan, et al., 2017; Kolluri, et al., 2016; Proebstle, et al., 2015; and Tekin, et al., 2016). A total of 1645 subjects were included in the studies, 691 underwent MOCA and 954 underwent CAVA. Rates were pooled using a random effects model. The pooled anatomic success for MOCA and cyanoacrylate ablation was 94.7% and 94.8% at six months and 94.1% and 89.0% at one year, respectively. Venous Clinical Severity score and Aberdeen Varicose Vein Questionnaire score significantly improved after treatment with MOCA and cyanoacrylate ablation. The authors noted that among the studies the definition of anatomic success varied, the use of adjunctive treatments varied, most of the studies had short term follow-up of six months to one year, and methodologic quality was only moderate. Although the results were promising the authors acknowledged high quality randomized controlled trials comparing these techniques with other well-established modalities are required.

DiMech et al. (2020) published their results of a systematic review evaluating 17 studies which met the inclusion criteria (RCTs, case reports, case series) for primary truncal veins and accessory tributaries, (n=2,910 patients [3,220 veins]). Within the studies a total of 1,981 subjects were administered VenaSeal, 445 underwent radiofrequency ablation (RFA), and 484 underwent endovenous laser ablation (EVLA). The mean procedure times were 25.7, 23.2, and 28.7 minutes, respectively. The mean recruitment period was 9 months (1-36 months) with an average follow-up of 12.3 months (1-36 months). A majority of veins were C2 to C3. The two-year occlusion rates were 93.7, 90.9, and 91.5% for VenaSeal, RFA, and EVLA, respectively.

Kolluri et al. (2020) published their results of a meta-analysis comparing VenaSeal with EVLT, RFA, MOCA, sclerotherapy and surgery as treatment of chronic venous insufficiency. A total of 20 RCTs were included in their review, comparing outcomes for the first six months of treatment. The primary outcome was anatomic success within 6 months. Secondary outcomes that were evaluated included ealth-related quality of life (HRQoL; EuroQol-5 Dimension, Aberdeen Varicose Vein Questionnaire), Venous Clinical Severity Score (VCSS), pain scores, and adverse events. Twenty RCTs including 4570 subjects were included in the analysis. For the primary outcome measure (anatomic success), VenaSeal system had the highest probability of being ranked first, RFA was second, EVLA third, surgery was fourth, MOCA fifth, and sclerotherapy was sixth. VenaSeal ranked third for secondary outcomes, fifth for quality of life outcome, and third for Aberdeen Varicose Vein score outcomes, and first for reduction of postoperative pain score from baseline. Odds of occurrence of adverse events was 3.3 times for sclerotherapy, 2.7 times for

EVLA and 1.1 time for surgery. Limitations include comparison of short term outcomes at six months and variable reporting methods by the authors.

Amshar et al. (2022) published the results of a systematic review and meta-analysis which included five studies, all conducted in Turkey, to evaluate the safety and efficacy of CAE in comparison to EVLA. Two of the studies included were RCTs and three were cohort studies. In total the studies were comprised of 1420 subjects with a total of 1432 interventions; 710 underwent CAE and 722 underwent EVLA, all with a minimum of one year follow-up. Outcomes of interest included efficacy as determined by venous occlusion rate and VCSS after one year, and safety which was determined by rates of periprocedural pain, skin pigmentation, nerve damage, phlebitis, deep vein thrombosis (DVT) and ecchymosis. Regarding efficacy the authors reported that pooled data of the RCTs showed a 95.8% occlusion rate at one year while the cohort studies showed a 94.2% occlusion rate; no significant differences were noted. A slight difference in VCCS was noted after one year between the CAE group and EVLA group, in both RCTs and cohort studies, favoring the CAE group, although it was not statistically different. The results tended to favor CAE when evaluating safety, whereas the CAE group was associated with less periprocedural pain score ($P < 0.001$), lower skin pigmentation rates (0.60% vs. 4.46%; $P = 0.008$), and lower nerve damage rates (0% vs. 3.94%; $P = 0.007$). Rates of phlebitis, deep vein thrombosis, and ecchymosis did not differ significantly between the 2 groups. It was additionally reported that intervention time was significantly faster in the CAE group in comparison to the EVLA group ($P < 0.001$). Limitations of the analysis include few studies that met inclusion criteria, studies limited to one country, one year outcomes, and lack of outcomes of interest reported in some studies.

Within an UpToDate review for nonthermal, nontumescent ablation techniques for the treatment of lower extremity superficial venous insufficiency the authors note that randomized trials that have compared cyanoacrylate adhesive ablation with radiofrequency venous ablation demonstrate similar outcomes and in one trial, longer-term (60 month) occlusion rates were improved for CAC compared with RFA (Scovell, et al, 2022).

Regarding short-term outcomes (12 months to 36 months) the body of evidence tends to support the efficacy of VenaSeal for treatment of saphenous vein incompetency. There is a growing body of evidence evaluating cyanoacrylate adhesive embolization in the peer-reviewed literature including systematic reviews, meta-analysis, observational and comparative trials (Amshar, et al., 2022; Guo, et al., 2021; Cho, et al., 2021; Dimech, et al., 2020; Kolluri, et al., 2020; Proebstle, et al., 2020, Garcia-Carpintero, et al., 2019; Kubat, et al., 2019 ; McGuinness, et al., 2019), that lend support to safety, efficacy and tolerability. In addition, several professional societies are supportive (European Society for Vascular Surgery, 2022; Ontario Health Quality, 2021; American Vein and Lymphatic Society, 2019; Australasion College of Phlebology, 2019). Although there remains a paucity of evidence to firmly establish long-term safety and efficacy of cyanoacrylate adhesive for treatment of varicose veins, the procedure does not require tumescent anesthesia and reported outcomes continue to support closure rates that are comparable to thermal ablative techniques, patient tolerance, few adverse events, and improved VCSS and Quality of Life Scores. While the adhesive is purported to break down over time, in at least one clinical trial it remained present at five years post procedure. Nevertheless, any resulting untoward effects remain unknown at this time.

Miscellaneous Treatments: Other proposed treatments for varicose veins, some only under investigation in countries outside the U.S., include but are not limited to endovenous steam ablation (EVSA) (Steam Vein Sclerosis System [SVS™, VenoSteam™], CermaVEIN, France); endovenous microwave ablation (Microwave Intracavitary Coagulation System, Fuzhong Medical High-Tech Co. Ltd., China), coil embolization, VariClose Vein Sealing System (Biolas, FG Group,Turkey) and endovenous catheter directed chemical ablation with balloon isolation.

Evidence confirming steam ablation and microwave ablation technologies have been approved or cleared for marketing by the FDA is lacking. In addition, much of the evidence evaluating these emerging modalities of treatment are in preliminary stages (Yang, et al., 2013; Milleret, et al., 2013; van den Bos, et al., 2014) and strong conclusions regarding safety and efficacy compared to well-established endovenous ablation treatments cannot be made at this time.

Evidence evaluating endovenous catheter directed chemical ablation with balloon isolation as a treatment of varicose veins was not found in the peer-reviewed published scientific literature. In theory adding occlusive balloon isolation to the vein wall may enhance the interaction of the sclerosant.

Coil embolization, also known as coil occlusion, involves the use of a coil combined with a sclerosant to occlude the vein and is under investigation for treatment of lower extremity varicose veins. It is a technique generally reserved for larger diameter veins such as perforating veins; the coil is curled up into the vein and may involve the use of more than one coil. Evidence in the peer-reviewed published literature evaluating this method of treatment for lower extremity varicosities is very limited (Viani, 2014), additional clinical trials are necessary to develop strong conclusions regarding safety and efficacy. A position statement published by Parsi, et al., 2020 supported by several professional societies (i.e., International Union of Phlebology [UIP], the Australasian College of Phlebology [ACP], the Australia and New Zealand Society for Vascular Surgery [ANZSVS, the American Venous Forum [AVF], the American Vein and Lymphatic Society [AVLS], and the Interventional Radiology Society of Australia [IRSA]) concludes that "there is no high-quality evidence to support the use of physical embolic agents such as coils, to treat axial venous reflux. The authors recommend against the use of such approaches for the treatment of saphenous incompetence outside of the clinical trial settings (Grade 2C Against).

External valvuloplasty is described as a reconstructive surgery to repair function of the terminal and preterminal valves to reduce vein diameter of the GSV and eliminate reflux. One method reported in the peer reviewed literature involves exposure of the GSV using an inguinal approach and application of a preformed, nonabsorbable polyurethane patch around the GSV (Muhlberger, et al, 2020, 2021). According to the authors a patch is held in place over the vein with sutures and is designed to reduce the diameter of the vein to ≤ 5mm in order to repair the valves (i.e., a diameter of 5mm is associated with a competent terminal valve in theory). In addition, multiple phlebectomies are performed on the side branches of the GSV. Eligibility criteria reported by this author group included individuals with a GSV diameter at the level of the saphenofemoral junction between 5-12 mm and valvular leaflets visible on Duplex US (n=359). At six month followup external valvuloplasty was considered sufficient if there was no reflux or occlusion of the GSV. A total of 210 subjects were available at followup (58%); valvuloplasty was considered sufficient in 95.4% of subjects. Limitations of this trial included high loss to followup, strict inclusion criteria, and lack of reflux measurements as noted by the authors. Currently there is insufficient evidence in the peer-reviewed scientific literature to support clinical efficacy and additional trials are needed.

Ambulatory selective ablation of varicose veins under local anesthetic (ASVAL) is a minimally invasive method of treatment for varicose veins based on "ascending theory" that venous disease evolves from the tributaries to the saphenous vein and then to the junction within the deep venous system. It has been described as primary surgical removal of the varicose reservoir by microavulsion of dilated and incompetent tributaries of the truncal vein that lie in the suprafascial venous network (isolated phlebectomy with sparing of the saphenous trunk) and is also referred to as a saphenous preserving intervention. In theory, ASVAL permits sparing of the incompetent GSV, reduces vein diameter, and subsequently reduces reflux. A major premise favoring the preservation of the GSV is the essential physiologic role that the GSV could play in superficial drainage and, to a lesser extent, its availability as revascularization material (Atavoy, Oguzkurt,

2016). Although the truncal vein may remain patent and become competent, recurrence rates have not been sufficiently studied and long term outcomes have not been reported. The European Society of Vascular Surgery reported that for individuals with uncomplicated varicose veins (i.e., CEAP clinical class C2) ASVAL may be considered however the recommendation is a Class IIb (Usefulness/efficacy is less well established by evidence/opinion., level of evidence C recommendation (i.e., consensus of opinion, small studies, retrospective studies and registries), and not strongly supported. Currently there is insufficient evidence in the peer-reviewed scientific literature to support patient selection criteria and clinical efficacy, additional trials are needed.

Professional Societies/Organizations
In 2023 the Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society published Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities. Within these guidelines they concluded the following regarding foam sclerotherapy specifically:

- For patients with symptomatic varicose veins and axial reflux in the GSV who place a high priority on the long-term outcomes of treatment (quality of life and recurrence), we suggest treatment with endovenous laser ablation, radiofrequency ablation, or high ligation and stripping over physician-compounded ultrasound-guided foam sclerotherapy because of long-term improvement of quality of life and reduced recurrence. GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: B (moderate, confidence in the treatment effect is moderate, additional research may or may not change the estimate of effect)
- 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 ultrasound-guided foam sclerotherapy, because of longterm improvement of quality of life and reduced recurrence GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (low to very low confidence in the treatment effect and additional research changing the estimate of the effect)
- 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 (quality of life and recurrence), we suggest treatment of the refluxing superficial trunk with endovenous laser ablation, radiofrequency ablation, or high ligation and stripping, with additional Journal Pre-proof 51 phlebectomy, if needed, over physician-compounded ultrasound-guided foam sclerotherapy, because of long-term improvement of quality of life and reduced recurrence GUIDELINE: Grade of recommendation: 2 (weak), Quality of Evidence: C (_low to very low confidence in the treatment effect and additional research changing the estimate of the effect).

The European Society for Vascular Surgery (ESVS) 2022 published clinical practice guidelines on the management of chronic venous disease of the lower limbs (De Maeseneer, et al., 2022). Within these guidelines the authors report that for patients with great saphenous vein incompetence requiring treatment, cyanoacrylate adhesive closure 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 less well established by evidence/opinion] Level of Evidence A (data from multiple RCTs or meta-analyses.

In 2021 Ontario Health Quality published "Nonthermal Endovenous Procedures for Varicose Veins: A Health Technology Assessment" which included 19 primary studies reported in 25 publications that compared either MOCA or CAC with at least one other invasive treatment for symptomatic varicose veins. It was noted that no studies compared MOCA with CAC. Within this document the authors reported that MOCA resulted in slightly poorer technical outcomes (vein closure and

recanalization) than thermal endovenous ablation procedures based on evidence of low to moderate quality. However, clinical outcomes, quality of life improvement, and patient satisfaction were similar compared with RFA (GRADE: Very low to Moderate) and EVLA (GRADE: High). Cyanoacrylate adhesive closure resulted in little to no difference in technical outcomes, clinical outcomes, and quality of life improvement compared with RFA and EVLA (GRADE: Moderate). Patient satisfaction may also be similar (GRADE: Low). Recovery time was slightly reduced with nonthermal endovenous procedures compared with thermal ablation (GRADE: Moderate). The effect of CAC compared with surgical vein stripping is very uncertain (GRADE: Very low). Major complications of any procedure were rare, with minor complications occurring as expected and resolving (Ontario Health Quality, 2021).

The American Venous Forum, the Society for Vascular Surgery, the American Vein and Lymphatic Society, and the Society of Interventional Radiology published appropriate use criteria (AUC) for chronic lower extremity venous disease (Masuda, et al., 2020). Within these recommendations the authors note the following are appropriate. Appropriateness was determined using the RAND/UCLA Appropriateness Method (RAM) for each scenario on the basis of a median rating and the agreement/disagreement of panelists. "Appropriate" was defined as being treatment that is a generally acceptable and reasonable approach for the indication and treatment which is likely to improve the patient's health outcomes or survival.

- Ablation of the GSV in a symptomatic patient with varicose veins, edema due to venous disease, skin or subcutaneous changes, healed or active ulcers (CEAP classes 2-6), when the GSV demonstrates axial reflux with or without SFJ reflux
- Ablation of the below-knee GSV in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers (CEAP classes 4-6), when there is segmental GSV reflux below the knee directed to the affected area.
- Ablation of the SSV in a symptomatic patient with varicose veins, edema due to venous disease, skin or subcutaneous changes, healed or active ulcers (CEAP classes 2-6), when the SSV demonstrates reflux directed to affected area
- Ablation of the SSV with reflux that communicates with the GSV or thigh veins by intersaphenous vein, in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers (CEAP classes 4-6), when the SSV demonstrates reflux directed to affected area
- Ablation of the AAGSV in a symptomatic patient with varicose veins, skin or subcutaneous changes, healed or active ulcers (CEAP classes 2, 4-6), when the AAGSV demonstrates axial reflux directed to affected area
- Treatment of nontruncal varicose veins with or without telangiectasia by sclerotherapy, ambulatory phlebectomy, or powered phlebectomy in a patient with symptomatic varicose veins, edema due to venous disease, skin or subcutaneous changes, healed or active ulcers (CEAP classes 2-6)
- Provide care for the diseased tributaries of an ablated saphenous vein either concomitantly or as a staged procedure (follow-up procedure) for clinical reasons
- Perforator vein treatment of veins with high outward flow and large diameter directed toward affected area in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers (CEAP classes 4-6)
- Scheduling the ablation of different veins on different days for clinical reasons including patient preference and safety is appropriate, whereas scheduling treatment on different days for reasons other than clinical reasons including patient preference and safety is not considered generally acceptable.

The American Vein and Lymphatic Society (previously the American College of Phlebology) published position statements in 2019 in support of both cyanoacrylate adhesive closure and MOCA as treatment of superficial venous disease when it is deemed to be medically necessary (American Vein and Lymphatic Society, 2019a, 2019b).

In 2014 guidelines for Endovenous Thermal Ablation (ETA) of the treatment of varicose veins were published by the First International Consensus Conference (Pavlovic, et al., 2014). Using a systematic literature review and expert opinion recommendations were made for endovenous thermal ablation procedures, which were defined as catheter-directed ultrasound-guided thermal methods (i.e., EVLA, RFA). The authors noted that there is little evidence evaluating other ablation procedures, such as steam ablation or bipolar RFA. Patient selection criteria varies depending on venous condition and general health, however veins applicable to endovenous thermal ablation include the GSV, SSV, accessory saphenous vein, Giacomini vein and cranial extension of SSV, superficial veins located in subcutaneous tissue, insufficient perforating veins, residual intrafascial veins following treatment, and venous malformations. Specific requirements for RFA include vein segment at least 10cm long using a standard catheter (7cm) or 5cm when a shorter heating element is used. No restrictions were noted for EVLA. Other recommendations in the guidelines addressed areas such as qualifications of ETA providers, pre and post treatment recommendations, indications, contraindications, generalized treatment plans and complications.

The American College of Phlebology (ACP) published revised guidelines for the treatment of superficial venous disease of the lower leg (ACP, 2014, rev 02/03/16). The updated guidelines are based on the 2011 review by Gloviczki et al., consensus of ACP experts, and current evidence. CEAP classification and VCSS (venous clinical severity score) were included in the revised guidelines to better define "medically significant venous insufficiency" versus what may be considered cosmetic and/or not medically necessary treatments. According to the guidelines indications for treatment include pain, edema, hemorrhage, recurrent superficial phlebitis, stasis dermatitis, or ulceration. CEAP classification and VCSS evaluation should be performed, with "medically necessary" being defined as a CEAP of C2 or higher. Duplex ultrasound is recommended prior to treatment with reflux time of > 500 msec regardless of vein diameter for the GSV, SSV, Anterior Accessory of the GSV, Posterior Accessory of the GSV, and Intersaphenous Vein (Vein of Giacomini). The ACP recommends (i.e., strong recommendation) treatment such as laser and radiofrequency ablation, open ligation and stripping for veins not amenable to endovenous procedures, stab phlebectomy, and liquid and foam chemical sclerotherapy with/without ultrasound guidance, as needed. Mechanical/chemical ablation (e.g., Clarivein) used to treat truncal reflux is a suggested treatment (i.e., weak recommendation [2B]). Treatment of incompetent perforator veins below a healed or open venous ulcer when reflux has an outward flow of 500 ms and a diameter is 3.5 cm is also a suggested treatment. In 2017 the American College of Phlebology Guidelines "Treatment of Refluxing Accessory Saphenous Veins" were published. Within these guidelines the authors acknowledged the FDA approvals for MOCA and cyanoacrylate glue does not exclude their use in accessory saphenous veins and that the Committee supports MOCA and cyanoacrylate techniques are likely effective for accessory saphenous veins although there are no case series published to date specifically evaluating efficacy in accessory veins. Treatment of accessory veins using endovenous thermal ablation of ultrasound guided foam sclerotherapy is as safe and effective as treatment of the GSV and SSV using the same modalities. Vein closure rates and improvement in quality of life scores are similar to results achieved with treatment of GSV and SSVs (Strength of Recommendation Grade 1, level of evidence C) (Gibson, et al., 2017).

In 2011 the Society for Vascular Surgery and the American Venous Forum (Gloviczki. et al., 2011) developed clinical practice guidelines for care of patients with varicose veins of the lower limbs and pelvis**.** Although not all-inclusive, the main recommendations of the committee may be summarized as follows:

- in patients with varicose veins or more severe chronic venous disease (CVD), a complete history and detailed physical examination are complemented by duplex ultrasound scanning of the deep and superficial veins

- the use of CEAP classification for patients with CVD and the revised Venous Clinical Severity Score to assess treatment outcome
- regarding Duplex scanning results:
  - a cutoff value of 1 second for abnormally reversed flow (reflux) in the femoral and popliteal veins
  - a cutoff value of 500 ms for abnormally reversed flow (reflux)for the great saphenous vein, the small saphenous vein, the tibial, deep femoral, and the perforating veins
  - in patients with chronic venous insufficiency, duplex scanning of the perforating veins is performed selectively; the definition of "pathologic" perforating veins includes those with an outward flow of duration of ≥ 500 ms, with a diameter of ≥ 3.5 mm and a location beneath healed or open venous ulcers (CEAP class C5-C6)
- compression therapy (pressure 20-30 mm Hg):
  - is suggested for patients with symptomatic varicose veins
  - as the primary treatment to aid healing of venous ulceration
  - in addition to ablation of incompetent superficial veins in order to decrease the recurrence of venous ulcers
  - is not recommended as the primary treatment if the patient is a candidate for saphenous vein ablation
- ligation and stripping for the treatment of incompetent great, small saphenous and superficial veins
- recommend the following:
  - endovenous thermal ablation (radiofrequency or laser) for treatment of incompetent saphenous vein rather than high ligation and inversion stripping of the saphenous vein to the level of the knee
  - phlebectomy or sclerotherapy to treat varicose tributaries
  - foam sclerotherapy as an option for the treatment of the incompetent saphenous vein (endovenous thermal ablation is recommended over foam sclerotherapy)
  - treatment of pathologic perforating veins (outward flow duration >500 ms, vein diameter >3.5 mm) located underneath healed or active ulcers (CEAP class C5-C6)
- recommend against selective treatment of perforating vein incompetence in patients with simple varicose veins (CEAP class C2).

Medicare Coverage Determinations

	Contractor	Policy Name/Number	Revision Effective Date
NCD	National	Not determination found	
LCD	National Government Services	Treatment of Varicose Veins of the Lower Extremity (L33575)	11/21/2019
LCD	CGS Administrators	Treatment of Varicose Veins of the Lower Extremity (L34082)	9/26/2019
LCD	Noridian	Treatment of Varicose Veins of the Lower Extremity (L34209)	12/01/2019
LCD	Wisconsin Physician Service	Treatment of Varicose Veins of the Lower Extremity (L34536)	9/3/2021

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

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

The treatment of varicose veins is covered only when coverage is available under the plan for varicose vein treatment. Benefit exclusions and limitations may apply. Invasive treatment of varicose veins is excluded under many plans and therefore the services listed below may not be covered.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

Ambulatory Phlebectomy

CPT®* Codes	Description
37765	Stab phlebectomy of varicose veins, 1 extremity; 10-20 stab incisions
37766	Stab phlebectomy of varicose veins, 1 extremity; more than 20 incisions
37799†	Unlisted procedure, vascular surgery

†**Note: Considered Medically Necessary when used to report stab phlebectomy of varicose veins, one extremity; less than 10 incisions.**

Ligation and Excision

CPT®* Codes	Description
37700	Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions
37718	Ligation, division, and stripping, short saphenous vein
37722	Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below
37735	Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia
37780	Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)
37785	Ligation, division, and/or excision of varicose vein cluster(s), 1 leg

Radiofrequency Ablation

CPT®* Codes	Description
36475	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated
36476	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)

Endovenous Laser Ablation

CPT®* Codes	Description
36478	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated
36479	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)

Endovascular Ablation Cyanoacrylate Adhesive (e.g., VenaSeal Closure System)

CPT®* Codes	Description
36482	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (eg, cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; first vein treated
36483	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (eg, cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)

Sclerotherapy

CPT®* Codes	Description
36470	Injection of sclerosant; single incompetent vein (other than telangiectasia)
36471	Injection of sclerosant; multiple incompetent veins (other than telangiectasia), same leg

HCPCS Codes	Description
S2202	Echosclerotherapy

Sclerotherapy using Ultrasound Guidance and a Microfoam Sclerosant (e.g., Varithena™):

CPT®* Codes	Description
36465	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; single incompetent extremity truncal vein (eg, great saphenous vein, accessory saphenous vein)
36466	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; multiple incompetent truncal veins (eg, great saphenous vein, accessory saphenous vein), same leg

Considered Cosmetic/ Not Medically Necessary:

Sclerotherapy for Treatment of Telangiectasia

CPT®* Codes	Description
36468	Injection(s) of sclerosant for spider veins (telangiectasia), limb or trunk

Intense Pulsed Light Source

CPT®* Codes	Description
17106	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); less than 10 sq cm
17107	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); 10.0 to 50.0 sq cm
17108	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); over 50.0 sq cm

Considered Experimental/Investigational/Unproven:

Transilluminated Powered phlebectomy (TIPP, TriVex™)

CPT®* Codes	Description
37799	Unlisted procedure, vascular surgery

Endomechanical Ablative Approach

CPT®* Codes	Description
36473	Endovenous ablation therapy of incompetent vein, extremity inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated
36474	Endovenous ablation therapy of incompetent vein, extremity inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
37241†	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicoceles)
37244	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for arterial or venous hemorrhage or lymphatic extravasation
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation

† **Note: In scope of this policy 37241 refers to varicose veins of the extremities.**

Endovenous Catheter Directed Chemical Ablation with Balloon Isolation

CPT®* Codes	Description
0524T	Endovenous catheter directed chemical ablation with balloon isolation of incompetent extremity vein, open or percutaneous, including all vascular access, catheter manipulation, diagnostic imaging, imaging guidance and monitoring

Coil Embolization

CPT®* Codes	Description
37241†	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicoceles)
37799	Unlisted procedure, vascular surgery

† **Note: In scope of this policy 37241 refers to varicose veins of the extremities.**

Considered Experimental/Investigational/Unproven when used to report cryostripping (including cryoablation, cryofreezing, and transilluminated cryosurgery), external valvuloplasty or ambulatory selective varicose vein ablation under local anesthetic (ASVAL):

CPT®* Codes	Description
37799	Unlisted procedure, vascular surgery

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Revision Details

Type of Revision	Summary of Changes	Date
Annual	Removed policy statement for subfascial endoscopic surgery.	11/15/2023