

# SURGICAL AND ABLATIVE PROCEDURES FOR VENOUS INSUFFICIENCY AND VARICOSE VEINS

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Community Plan Policy
<ul style="list-style-type: none"> <li>• <a href="#">Surgical and Ablative Procedures for Venous Insufficiency and Varicose Veins</a></li> </ul>

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## INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Medical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Medical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

## BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable. Some states require benefit coverage for services that UnitedHealthcare considers cosmetic procedures.

### Coverage Limitations and Exclusions

The following procedures are excluded from coverage:

- Procedures that correct an anatomical Congenital Anomaly without improving or restoring physiologic function are considered Cosmetic Procedures and therefore excluded from coverage. The fact that a Covered Person may suffer psychological consequences or socially avoidant behavior as a result of an Injury, Sickness or Congenital Anomaly does not classify surgery (or other procedures done to relieve such consequences or behavior) as a reconstructive procedure.
- Any procedure that does not meet the criteria in the [Coverage Rationale](#) section below.
- Treatments for Spider Veins and/or Telangiectasias are considered to be cosmetic and therefore excluded from coverage.
- Endovenous Ablation (radiofrequency and/or laser) of either reticular or telangiectatic veins is not reconstructive and not medically necessary and therefore excluded from coverage.

### Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten

categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

## COVERAGE RATIONALE

### **Varicose Vein Ablative and Stripping Procedures**

**Radiofrequency ablation, endovenous laser ablation, Stripping, Ligation and excision of the Great Saphenous Vein and Small Saphenous Veins are considered reconstructive, proven and medically necessary when ALL of the following criteria are present:**

- Junctional Reflux (see [Definitions](#) section):
  - Ablative therapy for the Great Saphenous Veins or Small Saphenous Veins will be considered reconstructive and therefore medically necessary only if Junctional Reflux is demonstrated in these veins; or
  - Ablative therapy for Accessory Veins will be considered reconstructive and medically necessary only if anatomically related persistent Junctional Reflux is demonstrated after the Great Saphenous Veins or Small Saphenous Veins have been removed or ablated.
- Member must have one of the following functional impairments:
  - Skin ulceration; or
  - Documented episode(s) of frank bleeding of the Varicose Vein due to erosion of/ or trauma to the skin; or
  - Documented Superficial Thrombophlebitis or documented Venous Stasis Dermatitis; or
  - Moderate to severe pain causing Functional/Physical Impairment.
- Venous Size:
  - The Great Saphenous Vein must be 5.5 mm or greater when measured at the proximal thigh immediately below the saphenofemoral junction via Duplex Ultrasonography.
  - The Small Saphenous Vein or Accessory Veins must measure 5 mm or greater in diameter immediately below the appropriate junction.
- Duration of reflux, in the standing or reverse Trendelenburg position that meets the following parameters:
  - Greater than or equal to 500 milliseconds (ms) for the Great Saphenous vein, Small Saphenous Veins or principle tributaries.
  - Perforating veins > 350 ms.
  - Some Duplex Ultrasound readings will describe this as moderate to severe reflux which will be acceptable.

**Ablation of perforator veins is considered reconstructive, proven and medically necessary when the following criteria are present:**

- Evidence of perforator Venous Insufficiency measured by recent Duplex Ultrasonography report (see criteria above); and
- Perforator vein size is 3.5 mm or greater; and
- Perforating vein lies beneath a healed or active venous stasis ulcer.

**Endovenous mechanochemical ablation (MOCA) of Varicose Veins using a percutaneous infusion catheter is unproven and not medically necessary for treating Venous Reflux.**

There is insufficient evidence in the clinical literature supporting the safety and efficacy of MOCA for treating Varicose Veins. Further results from large, well-designed studies are needed to support the clinical utility of this approach.

### **Ligation Procedures**

**Ligation of the Great Saphenous Vein at the saphenofemoral junction, as a stand-alone procedure, is unproven and not medically necessary for treating venous reflux.**

Ligation performed without Stripping or ablation is associated with high long-term recurrence rates due to neovascularization.

**Ligation of the Small Saphenous Vein at the saphenopopliteal junction, as a stand-alone procedure, is unproven and not medically necessary for treating Venous Reflux.**

Ligation performed without Stripping or ablation is associated with high long-term recurrence rates due to neovascularization.

**Ligation at the saphenofemoral junction, as a stand-alone procedure, is proven and medically necessary, when used to prevent the propagation of an active clot to the deep venous system in individuals with ascending Superficial Thrombophlebitis who fail or are intolerant of anticoagulation therapy.**

**Ligation at the saphenofemoral junction, as an adjunct to radiofrequency ablation or endovenous laser ablation of the main saphenous veins, is unproven and not medically necessary for treating Venous Reflux.**

Published clinical evidence has not demonstrated that the addition of saphenofemoral ligation to Endovenous Ablation procedures provides an additive benefit in resolving Venous Reflux or preventing Varicose Vein recurrence. Endovenous Ablation is a clinically effective therapy for treating Venous Reflux. Adding Ligation to the procedure adds clinical risk without adding clinical benefit.

**Endovascular embolization of Varicose Veins using [cyanoacrylate-based adhesive](#) is unproven and not medically necessary for treating Venous Reflux.**

There is insufficient evidence in the published clinical literature supporting the safety and efficacy of endovascular embolization using cyanoacrylate-based adhesive for treating Varicose Veins. Further long-term results from large, well-designed studies are needed to support the clinical utility of this approach.

**[Endovenous foam sclerotherapy](#) of incompetent Great Saphenous Veins, lesser saphenous veins, and accessory saphenous veins is unproven and not medically necessary for treating Venous Reflux.**

There is insufficient evidence in the published clinical literature supporting the safety and efficacy of endovascular embolization using endovenous foam sclerotherapy for treating Varicose Veins. Further long-term results from large, well-designed studies are needed to support the clinical utility of this approach.

## DEFINITIONS

**When applicable, please refer to the member specific benefit plan document for definitions.**

**Accessory/Tributary Vein:** Axial accessory or tributary saphenous veins indicate any venous segment ascending parallel to the Great Saphenous Vein and located more superficially above the saphenous fascia, both in the leg and in the thigh. These can include the anterior Accessory Vein, the postero-medial vein, circumflex veins [anterior or posterior], intersaphenous veins, Giacomini vein or posterior [Leonardo] or anterior arch veins.

**Congenital Anomaly:** A physical developmental defect that is present at the time of birth, and that is identified within the first twelve months of birth (2017 Generic COC).

**Congenital Anomaly (California only):** A physical developmental defect that is present at birth (2017 Generic COC).

**Cosmetic Procedures:** Procedures or services that change or improve appearance without significantly improving physiological function, as determined by us (2017 Generic COC).

**Cosmetic Procedures (California only):** Procedures or services that are performed to alter or reshape normal structures of the body in order to improve the Covered Person's appearance (2017 Generic COC).

**Duplex Ultrasonography:** Combines a real-time B mode scanner with built-in Doppler capability. The B mode scanner outlines anatomical structure while Doppler detects the flow, direction of flow and flow velocity.

**Duplicate Saphenous Vein:** True duplication of a saphenous vein is rare. The saphenous veins are found in the saphenous canal or fascial envelope, which is bounded by the superficial and deep fascia. A true dual system occurs when both veins are found inside the saphenous canal. A second vein that runs parallel to the saphenous vein, but outside the saphenous canal, is considered an [Accessory Vein](#) (Cronenwett and Johnston, 2014).

**Endovenous Ablation:** A minimally invasive procedure that uses heat generated by radiofrequency (RF) or laser energy to seal off damaged veins.

**Functional/Physical Impairment:** A Functional/Physical Impairment or physiological impairment causes deviation from the normal function of a tissue or organ. This results in a significantly limited, impaired, or delayed capacity to move, coordinate actions, or perform physical activities and is exhibited by difficulties in one or more of the following areas: physical and motor tasks; independent movement; performing basic life functions.

**Great Saphenous Vein (GSV):** The GSV originates from the dorsal arch of the foot and progresses medially and proximally along the distal extremity to join the common femoral vein.

**High Quality Photograph:** Ideally, a high-quality print should be in color have at least 200 pixels per inch. It must be detailed enough to show the individual's anatomy that is described in the physician's office notes. If submitted as a hard copy, the image must be on photographic paper.

**Junctional Reflux:** Reflux that exceeds a duration of 0.5 seconds at either:

- The saphenofemoral junction (SFJ) – Confluence of the Great Saphenous Vein and the femoral vein; or
- The saphenopopliteal junction (SPJ) – Confluence of the Small Saphenous Vein and the popliteal vein.

**Ligation:** Tying off a vein.

**Reconstructive Procedures:** Reconstructive procedures when the primary purpose of the procedure is either of the following:

- Treatment of a medical condition.
- Improvement or restoration of physiologic function.

Reconstructive procedures include surgery or other procedures which are related to an Injury, Sickness or Congenital Anomaly. The primary result of the procedure is not a changed or improved physical appearance.

Procedures that correct an anatomical Congenital Anomaly without improving or restoring physiologic function are considered Cosmetic Procedures. The fact that you may suffer psychological consequences or socially avoidant behavior as a result of an Injury, Sickness or Congenital Anomaly does not classify surgery (or other procedures done to relieve such consequences or behavior) as a reconstructive procedure (2017 COC).

**Reconstructive Procedures (California only):** Reconstructive procedures to correct or repair abnormal structures of the body caused by congenital defects, developmental abnormalities, trauma, infection, tumors, or disease to do either of the following:

- To improve function.
- To create a normal appearance, to the extent possible.

Reconstructive procedures include surgery or other procedures which are associated with an Injury, Sickness or Congenital Anomaly. The primary result of the procedure is not a changed or improved physical appearance for cosmetic purposes only, but rather to improve function and/or to create a normal appearance, to the extent possible (2017 COC).

**Reticular Vein:** Reticular Veins are dilated dermal veins less than 4mm in diameter that communicate with either or both Telangiectasia and saphenous tributaries.

**Sickness:** Physical illness, disease or Pregnancy. The term Sickness includes Mental Illness or substance-related and addictive disorders, regardless of the cause or origin of the Mental Illness or substance-related and addictive disorder (2017 COC).

**Small Saphenous Vein:** Superficial vein of the calf.

**Spectral Doppler Flow Imaging:**

- Examines flow at one site.
- Provides a detailed analysis of distribution of flow.
- Provides good temporal resolution, capable of examining flow waveform.
- Allows for calculation of velocity and indices.

**Spider Vein:** Spider Veins/Telangiectasia are the permanent dilation of preexisting small blood vessels, generally up to 1mm in size.

**Stripping:** Surgical removal of superficial veins.

**Superficial Thrombophlebitis:** Inflammation of a vein due to a blood clot in a vein just below the skin's surface.

**Telangiectasia:** See [Spider Vein](#).

**Varicose Veins:** Abnormally enlarged veins that are frequently visible under the surface of the skin; often appear blue, bulging and twisted.

**Venous Reflux/Insufficiency:** Venous Reflux is reversed blood flow in the veins [away from the heart]. Abnormal [pathological reflux] is defined as reverse flow that lasts beyond a specified period of time as measured by Doppler ultrasound. Normal [physiological reflux] is defined as reverse flow that lasts less than a specified period of time as measured by Doppler ultrasound. Abnormal [pathological reflux] times exceed different thresholds depending on the system of veins:

- Deep veins: 1 sec

- Superficial veins: 0.5 sec
- Perforator veins: 0.35 sec

**Venous Stasis Dermatitis:** A skin inflammation due to the chronic buildup of fluid (swelling) under the skin.

#### APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

**Coding Clarification:** According to the American Medical Association (AMA), CPT code 37241 is specific to venous embolization/occlusion and excludes lower extremity venous incompetency. Coding instructions state that 37241 should not be used to report treatment of incompetent extremity veins. For sclerosis of veins or endovenous ablation of incompetent extremity veins, see 36468-36479 (CPT Assistant, 2014).

CPT Code	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 (e.g., 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 (e.g., great saphenous vein, accessory saphenous vein), same leg
36473	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated
36474	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36475	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated
36476	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36478	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated
36479	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36482	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (e.g., 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 (e.g., 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)
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

CPT Code	Description
37780	Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)
37799	Unlisted procedure, vascular surgery

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## DESCRIPTION OF SERVICES

Varicose Veins are enlarged veins that are swollen and raised above the surface of the skin. They can be dark purple or blue, and look twisted and bulging. Varicose Veins are commonly found on the backs of the calves or on the inside of the leg. Veins have one-way valves that help keep blood flowing towards the heart. When the valves become weak or damaged and do not close properly, blood can back up and pool in the veins causing them to get larger. The resulting condition is known as Venous Insufficiency or Venous Reflux. Varicose Veins may lead to complications such as pain, blood clots or skin ulcers.

Varicose Veins are treated with lifestyle changes and medical procedures done either to remove the veins or to close them. Endovenous Ablation therapy uses lasers or radiofrequency energy to create heat to close off a Varicose Vein. Vein Stripping and Ligation involves tying shut and removing the veins through small cuts in the skin (National Heart, Lung and Blood Institute [NHLBI], 2014).

Endomechanical ablation uses a specialized, rotating catheter (e.g., ClariVein) to close off a Varicose Vein by damaging the vessel lining prior to injecting a sclerosing agent. This technique is also referred to as mechanochemical ablation (MOCA), mechanico-chemical endovenous ablation (MCEA) and mechanically enhanced endovenous chemical ablation (MEECA).

Endovascular embolization using cyanoacrylate-based adhesive (e.g., VenaSeal™ Closure System) is a minimally invasive, non-thermal and non-sclerosant procedure that does not require tumescent anesthesia. The medical adhesive is used to close the lower extremity superficial truncal veins, such as the Great Saphenous Vein, in individuals with symptomatic Venous Reflux disease.

Endovascular embolization using endovenous foam sclerotherapy with polidocanol endovenous microfoam (PEM) (e.g., Varithena™ [Provensis Ltd.]), is a prescribed proprietary canister that generates a sterile, uniform, stable, low-nitrogen polidocanol 1% microfoam sclerosant intended for ultrasound-guided intravenous (IV) injection for treating venous incompetence and varicosities (Hayes, 2016). The aim of ultrasound-guided foam sclerotherapy for Varicose Veins is to damage the endothelial surface of the vein causing scarring and leading to blockage of the treated Varicose Veins. Sclerosant, in the form of a foam, is intended to have good surface area contact with the vein walls (National Institute of Health and Care Excellence [NICE], 2013).

## CLINICAL EVIDENCE

In a meta-analysis, Hamann et al. (2017) compared the long-term efficacy of different treatment modalities for varicose veins (high ligation with stripping (HL+S), endovenous thermal ablation (EVTA), mainly consisting of endovenous laser ablation (EVLA) or radiofrequency ablation, and ultrasound guided foam sclerotherapy (UGFS). Three randomized controlled trials (RCTs) and 10 follow-up studies of RCTs with follow-up ≥ 5 years were included. In total, 611 legs were treated with EVLA, 549 with HL+S, 121 with UGFS, and 114 with HL+EVLA. UGFS had significantly lower pooled anatomical success rates than HL+S, EVLA, and EVLA with high ligation: 34% (95% CI 26-44) versus 83% (95% CI 72-90), 88% (95% CI 82-92), and 88% (95% CI 17-100) respectively;  $p \leq .001$ . The pooled recurrent reflux rate at the SFJ was significantly lower for HL+S than UGFS (12%, 95% CI 7-20, vs. 29%, 95% CI 21-38;  $p \leq .001$ ) and EVLA (12%, 95% CI 7-20, vs. 22%, 95% CI 14-32;  $p = .038$ ). VCSS scores were pooled for EVLA and HL+S, which showed similar improvements. Based on the results of the meta-analysis, EVLA and HL+S show higher success rates than UGFS 5 years after GSV treatment. Recurrent reflux rates at the SFJ were significantly lower in HL+S than UGFS and EVLA. VCSS scores were similar between EVLA and HL+S.

Boersma et al. (2016) performed a systematic review and meta-analysis of treatment modalities for small saphenous vein insufficiency. The review included 49 studies (5 randomized controlled trials, 44 cohort studies) reporting on the different treatment modalities: surgery (n=9), endovenous laser ablation (EVLA) (n=28), radiofrequency ablation (RFA) (n=9), ultrasound-guided foam sclerotherapy (UGFS) (n=6) and MOCA (n=1). The primary outcome of anatomical success was defined as closure of the treated vein on follow-up duplex ultrasound imaging. Secondary outcomes were technical success and major complications. The pooled anatomical success rate was 58.0% for surgery in 798 veins, 98.5% for EVLA in 2950 veins, 97.1% for RFA in 386 veins and 63.6% for UGFS in 494 veins. One study reported results of MOCA, with an anatomical success rate of 94%. Neurologic complications were most frequently reported after surgery and thermal ablation. Deep venous thrombosis was a rare complication. The authors concluded that EVLA and RFA are preferred to surgery and foam sclerotherapy in the treatment of small saphenous vein

insufficiency. Although data on nonthermal techniques is still sparse, the potential benefits, especially the reduced risk of nerve injury, might be of considerable clinical importance.

O'Hare et al. (2008) conducted a multicenter, prospective cohort study of patients undergoing small saphenous vein surgery (SSV). Patients were evaluated at six weeks and one year after surgery. A total of 204 legs were reviewed at one year; 67 had small saphenous varicose vein stripping, 116 had saphenopopliteal junction (SPJ) disconnection only and the remainder had miscellaneous procedures. The incidence of visible recurrent varicosities at one year was lower after SSV stripping than after disconnection only, although this did not reach statistical significance. The rate of SPJ incompetence detected by duplex at one year was significantly lower in patients who underwent SSV stripping than in those who did not.

In a 5-year follow-up from two randomized controlled trials, Rass et al. (2015) compared the long-term clinical efficacy of endovenous laser ablation (EVLA) with high ligation and stripping (HLS) as standard treatment for great saphenous vein (GSV) incompetence. Two hundred and eighty one legs (81% of the study population) were evaluated with a median follow up of 60.4 (EVLA) and 60.7 months (HLS). Overall, REVAS was similarly observed in both groups: 45% (EVLA) and 54% (HLS),  $p = .152$ . Patients of the EVLA group showed significantly more clinical recurrences in the operated region (REVAS: same site): 18% vs. 5%,  $p = .002$ . In contrast, an increase in different site recurrences was observed in the HLS group: 50% vs. 31%,  $p = .002$ . Duplex detected saphenofemoral refluxes occurred more frequently after EVLA: 28% vs. 5%,  $p < .001$ . Both treatments improved disease severity and quality of life without any difference. The authors concluded that EVLA and HLS are comparably effective concerning overall REVAS, improvement of disease severity, and quality of life. In terms of same site clinical recurrence and saphenofemoral refluxes, HLS is superior to EVLA 5 years after treatment.

Gauw et al. (2016) evaluated 5-year outcomes from a randomized, controlled trial to compare the long-term results (groin-related recurrence, great saphenous vein [GSV] occlusion rate, clinical class, etiology, anatomy, and pathophysiology [CEAP] staging, and quality of life [QoL]) after the treatment of a GSV incompetence by saphenofemoral ligation and stripping (SFL/S) with endovenous laser ablation bare fiber, 980 nm (EVLA). Patients ( $n=121$ ; 130 legs) with GSV insufficiency and varicose veins were randomized to either undergo SFL/S or EVLA. At the 5-year follow-up, a significantly higher varicose vein recurrence rate originated at the SFJ region after EVLA compared with SFL/S. There were no differences in the relief of venous symptoms, CEAP staging, or general QoL between the groups.

In a multicenter, randomized controlled trial with up to 6 years follow-up, Flessenkämper et al. (2016) compared high ligation and stripping to endovenous laser ablation for the therapy of great saphenous vein varicosity. Patients ( $n=449$ ) were randomized into three different treatment groups: high ligation and stripping group ( $n = 159$ ), endovenous laser ablation group ( $n = 142$ ; 980 nm, 30 W continuous mode, bare fiber) or a combination of laser ablation with high ligation (endovenous laser ablation group/ high ligation group,  $n = 148$ ). The authors observed that clinical recurrence appears with the same frequency in all three treatment groups, but the responsible pathological mechanisms seem to differ. Most reflux into the great saphenous vein and side branches appears after endovenous laser ablation, whereas more saphenofemoral junction-independent recurrences are seen after high ligation/stripping.

In a literature review of long-term results following high ligation supplemented by sclerotherapy, Recek (2004) found that ligation of the saphenofemoral junction alone provokes a higher recurrence rate in comparison with high ligation and stripping. The hemodynamic improvement achieved immediately after high ligation deteriorates progressively during the follow-up owing to recurrent reflux.

Woźniak et al. (2016) conducted a quantitative-qualitative analysis of complications and failure of endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) in a 5-year follow-up. One hundred ten adult participants with varicose veins clinical grade C2 to C6, treated for isolated great saphenous vein (GSV) or small saphenous vein (SSV) insufficiency in a single lower extremity in 2009 to 2010, were enrolled and subdivided into EVLA ( $n=56$ ) and RFA ( $n=54$ ) groups. Both groups were compared for demography, disease stage, affected veins, perioperative, and postoperative complications as well as treatment efficacy. The perioperative and postoperative complications were statistically insignificant. Treatment efficacy, expressed as the number of participants with recurrent varicosity and recanalization, was comparable in both groups. The clinically significant recanalization rate was 3.6% and 5.6% in EVLA and RFA groups, respectively. The authors concluded that EVLA and RFA for the management of lower extremity varicose vein offer comparable efficacy and safety in a 5-year follow-up.

In a systematic review and meta-analysis of randomized controls of endovenous ablation (EVA) of the great saphenous vein (GSV), O'Donnell et al. (2016) evaluated recurrence and cause of varicose veins after surgery (REVAS). Seven RCTs provided eight comparisons (one study compared both types of EVA to a comparator arm): three used radiofrequency ablation, and five employed endovenous laser ablation. Overall recurrent varicose veins developed in 125 limbs after EVA (22%), with no difference in the incidence vs the ligation and stripping (L&S) group (22%) based on the number of limbs available at the time of the development of recurrence for both groups, but this

incidence is dependent on the length of follow-up after the initial treatment. Neovascularization occurred in only two limbs (2%) after EVA vs 18 (18%) in the L&S group. Recanalization was the most common cause of REVAS for EVA (32%; 40 of 125 limbs), followed by the development of anterior accessory saphenous vein incompetence (19%; 23 of 125 limbs). The authors concluded that there is no difference in the incidence of REVAS for EVA vs L&S, but the causes of REVAS are different with L&S.

Wichers et al. (2005) performed a systematic review of randomized trials evaluating the safety and efficacy of medical (anticoagulants) or surgical (ligation or stripping of the affected veins) treatments of superficial vein thrombosis (SVT) for the prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE). Five studies were included. Pooling of the data was not possible due to the heterogeneity among the studies. Three studies had major methodological drawbacks limiting the clinical applicability of the results. One of the remaining (pilot) studies showed a non-significant trend in favor of high-compared to low-dose unfractionated heparin for the prevention of venous thromboembolism (VTE). The last remaining study showed a non-significant trend in favor of short-term treatment with low-molecular-weight heparin (LMWH) or a non-steroidal anti-inflammatory drug (NSAID) as compared to placebo shortly after treatment with respect to VTE, but the apparent benefit disappeared after three months of follow-up. More randomized controlled trials are needed before any evidence-based recommendations on the treatment of SVT for the prevention of VTE can be given. With the lack of solid evidence, the authors suggest treating patients with at least intermediate doses of LMWH. Surgical treatment of SVT may be considered when varicose veins are involved.

Sullivan et al. (2001) performed a systematic review of the literature evaluating surgical and medical management of above-knee superficial thrombophlebitis (AK-STP) not involving the deep venous system. Six studies were included for a total of 246 patients in the surgical arm and 88 patients in the medical arm. Surgical treatment modalities halt the progression of thrombus into the deep venous system through the saphenofemoral junction and reduce the incidence of PE. The two types of surgical treatment were ligation of the great saphenous vein at the saphenofemoral junction or ligation in combination with stripping of the phlebitic vein. Medical therapy consisted of initial intravenous heparin followed by warfarin therapy for a duration varying between 6 weeks and 6 months. The authors offered no definitive conclusions due to reporting of varied outcomes, different follow-up criteria and the retrospective nature of the studies. The differences between the surgical and medical groups were small. The review concludes that medical management with anticoagulants is superior for minimizing complications and preventing subsequent deep vein thrombosis and pulmonary embolism development as compared to surgical treatment with ligation of the great saphenous vein at the saphenofemoral junction or ligation and stripping.

Winterborn et al. (2004) conducted an 11 year follow-up study on the Jones et al. patient group. A cumulative total of 83 legs had developed clinically recurrent varicose veins by 11 years (62%). There was no statistically significant difference between the ligation-only and the stripping groups. Reoperation was required for 20 of 69 legs that underwent ligation alone compared with 7 of 64 legs that had additional long saphenous vein stripping. Freedom from reoperation at 11 years was 70% after ligation, compared with 86% after stripping. The presence of neovascularization, an incompetent superficial vessel in the thigh or an incompetent saphenofemoral junction on duplex imaging at 2 years postoperatively increased the risk of a patient's developing clinically recurrent veins. Results from the study indicate that stripping the long saphenous vein is recommended as part of routine varicose vein surgery as it reduces the risk of reoperation after 11 years, although it did not reduce the rate of visible recurrent veins.

In a systematic review, Darwood and Gough (2009) found that adjunctive saphenofemoral ligation is not necessary to achieve success with endovenous laser therapy of the great saphenous vein. Similarly, a randomized controlled trial conducted by Disselhoff et al. (2008) found that the addition of saphenofemoral ligation to endovenous ablation made no difference to the short-term outcome of varicose vein treatment. Long-term follow-up at 5 years found similar results (Disselhoff et al. 2011). Further studies with larger patient populations are needed to establish the superiority of adjunctive saphenofemoral ligation in improving long-term outcomes.

Theivacumar et al. (2007) also found that saphenofemoral ligation following endovenous laser ablation was unnecessary. Persistent non-refluxing great saphenous vein tributaries at the saphenofemoral junction did not have an adverse impact on clinical outcome 1 year after successful endovenous laser ablation of the great saphenous vein.

### **Endovenous Mechanochemical Ablation**

Kim et al. (2017) evaluated whether early efficacy in endovenous mechanochemical ablation (MOCA) is maintained at 24 months. Patients with reflux in the great saphenous vein involving the sapheno-femoral junction and no previous venous interventions were included. The occlusion rate of treated veins was assessed with duplex ultrasound. Patient clinical improvement was assessed by Clinical-Etiology-Anatomy-Pathophysiology (CEAP) class and venous clinical severity score. Of the initial 126 patients, there were 65 patients with 24 month follow-up. Of these 65 patients, 70% were female, with a mean age of  $70 \pm 14$  years and an average BMI of  $30.5 \pm 6$ . The mean great saphenous vein diameter in the upper thigh was 7.6 mm and the mean treatment length was 39 cm. Adjunctive treatment of the



varicosities was performed in 14% of patients during the procedure. Closure rates were 100% at one week, 98% at three months, 95% at 12 months, and 92% at 24 months. There was one patient with complete and four with partial recanalization ranging from 7 to 12 cm (mean length 9 cm). There was significant improvement in CEAP and venous clinical severity score ( $P < .001$ ) for all time intervals. Early high occlusion rate with mechanochemical ablation is associated with significant clinical improvement which is maintained at 24 months, which according to the authors, is suggestive of a good option for the treatment of great saphenous vein incompetence. Longer-term outcomes are needed to evaluate MOCA's efficacy.

Witte et al. (2017) reported midterm results of MOCA for treating great saphenous vein (GSV) insufficiency. In a 1-year period, 85 consecutive patients undergoing MOCA with polidocanol in 104 limbs were enrolled in a prospective registry. The patients were evaluated at baseline and during follow-up (4 weeks and 1, 2, and 3 years) using duplex ultrasound, the CEAP (clinical, etiologic, anatomic and pathophysiologic) classification, the Venous Clinical Severity Score (VCSS), the RAND Short Form 36-Item Health Survey (RAND-SF36), and the Aberdeen Varicose Vein Questionnaire (AVVQ). Primary outcome measures were clinical and anatomic success. Secondary outcome measures included general and disease-specific quality of life and re-interventions. After a median follow-up of 36 months (interquartile range 12.5, 46.3), recanalization occurred in 15 (15%) of 102 successfully treated vein segments. Anatomic success was 92%, 90%, and 87% after 1, 2, and 3 years, respectively. The VCSS improved at all time intervals compared to the preprocedure median. The clinical success at 3 years was 83%. The AVVQ and RAND-SF36 scores showed an improvement at all time intervals compared to baseline values. Between 12 and 36 months, however, a significant deterioration was observed in VCSS, which was accompanied by worsening of disease-specific and general quality of life. Although the authors concluded that MOCA demonstrated to be an effective treatment modality for GSV insufficiency at midterm follow-up, clinical results seemed to drop over time.

In a systematic review and meta-analysis to compare traditional surgery and endovenous laser ablation (EVLA) for the treatment of venous insufficiency of the great saphenous veins, Quarto et al. (2016) evaluated 756 legs treated with a conventional surgical procedure and 755 legs treated with EVLA. Only RCTs based at least on 6 months follow-up were considered eligible in the study. The authors did not find a statistically significant difference in the presence or absence of reflux between the two techniques, and noted that although EVLA did not prove to be superior in terms of recurrence to the surgical technique, EVLA remains a viable treatment option in patients with impaired great saphenous vein, reducing postoperative pain and hospital stay.

Go et al. (2016) reviewed the cases of 24 limbs of 17 patients who underwent EVLA between 2004 and 2007 that were examined with duplex ultrasonographic scans at a mean follow-up of 66 months. There were five recurrences of saphenofemoral junction reflux. The occlusion rate was 79.2% at a mean follow-up of 66.1 months. There were 14 recanalizations and 5 recurrences of the great saphenous vein. Five partial and nine total recanalizations were observed. The authors concluded that EVLA is an effective and minimally invasive treatment for varicose veins and although their long-term result was acceptable, the result was not outstanding. A study limitation was the small patient population.

Bootun et al. (2016) compared pain scores in patients treated for primary varicose veins. A total of 119 patients were randomized to mechanochemical ablation ( $n=60$ ) or radiofrequency ablation ( $n=59$ ). Maximum pain score was significantly lower in the mechanochemical ablation group compared to the radiofrequency ablation group. Average pain score was also significantly lower in the mechanochemical ablation group compared to the radiofrequency ablation group. Sixty-six percent attended follow-up at one month, and the complete or proximal occlusion rates were 92% for both groups. At one month, the clinical and quality of life scores for both groups had similar improvements. The long-term data including occlusion rates at six months and quality of life scores are being collected.

Bishawi et al. (2014) conducted a prospective observational multicenter study on the efficacy of MOCA in patients with lower extremity chronic venous disease. A total of 126 patients were included at baseline, 81% females. The mean diameter of the great saphenous vein in the upper thigh was 7.3 mm and the mean treatment length was 38 cm. Adjunctive treatment was performed in 11% of patients during the procedure. Closure rates were 100% at one week, 98% at three months and 94% at six months. Post-procedure complications included hematoma, ecchymosis and thrombophlebitis. There were no cases of venous thromboembolism. The authors concluded that MOCA of the saphenous veins has the advantage of endovenous ablation without tumescent anesthesia. This study is limited by lack of randomization and control and short-term follow-up.

Vun et al. (2015) assessed the efficacy of the ClariVein system for the treatment of superficial vein incompetence. Fifty-one great saphenous veins and six small saphenous veins were treated. Duplex showed a technical success rate of 91%. Comparison with 50 RFA and 40 EVLA procedures showed procedure times were significantly less for ClariVein than for either RFA or EVLA. Median pain scores were significantly lower for ClariVein than for RFA and EVLA. No major complications or deep vein thromboses were reported. Study limitations included small sample size, lack of randomization and control and short-term follow-up. Further data on long-term clinical outcomes is needed.

In a prospective comparison study, van Eekeren et al. (2013) evaluated postoperative pain and quality of life after radiofrequency ablation (RFA) and MOCA for great saphenous vein (GSV) incompetence. Sixty-eight patients with unilateral GSV incompetence were included. Patients treated with MOCA reported significantly less postoperative pain than patients treated with RFA during the first 14 days after treatment. The lower postoperative pain score was associated with a significantly earlier return to normal activities and work. At 6 weeks, patients in both groups perceived an improved change in health status and an improved disease-specific quality of life. This study is limited by lack of randomization and control, small sample size and short-term follow-up.

In a prospective cohort study, Boersma et al. (2013) evaluated the feasibility, safety and 1-year results of MOCA of small saphenous vein (SSV) insufficiency. Fifty consecutive patients were treated using the ClariVein device and polidocanol. At the 6-week assessment, all treated veins were occluded. One-year follow-up showed a 94% anatomic success rate and no major complications. The authors concluded that MOCA is a safe, feasible and efficacious technique for treating SSV insufficiency. This study is limited by lack of randomization and control, small sample size and short-term follow-up.

Elias and Raines (2012) assessed the safety and efficacy of the ClariVein<sup>®</sup> system for mechanochemical ablation of the great saphenous vein (GSV). Thirty GSVs in 29 patients were treated. At six-month follow-up, the primary closure rate was 96.7% with no adverse events reported. The authors concluded that mechanochemical ablation appears to be safe and efficacious. This study is limited by lack of randomization and control, small sample size and short-term follow-up.

In a pilot study, Van Eekeren et al. (2011) evaluated the feasibility and safety of endovenous MOCA for the treatment of great saphenous vein (GSV) incompetence. Thirty limbs in 25 patients (18 women; mean age 52 years) with GSV incompetence were treated with the ClariVein<sup>®</sup> device. Initial technical success, complications, patient satisfaction and classification by venous clinical severity score (VCSS) were assessed 6 weeks after the treatment. Initial technical success of MOCA was 100%. There were no major adverse events. Duplex ultrasonography at 6 weeks showed 26 (87%) of 30 veins were completely occluded. Three veins showed partial recanalization in the proximal and distal GSV. One patient had full segment recanalization and was successfully retreated. The VCSS significantly improved at 6 weeks. Patient satisfaction was high, with a median satisfaction of 8.8 on a 0-10 scale. The authors concluded that endovenous MOCA is feasible and safe in the treatment of GSV incompetence. Larger studies with a prolonged follow-up are indicated to prove the efficacy of this technique.

In an updated guideline on endovenous mechanochemical ablation for varicose veins, the National Institute for Health and Care Excellence (NICE) (2016) states that current evidence on the safety and efficacy of endovenous mechanochemical ablation for varicose veins appears adequate to support the use of this procedure provided that standard arrangements are in place for consent, audit and clinical governance. Clinicians are encouraged to collect longer-term follow-up data.

### **Endovascular Embolization with Cyanoacrylate-Based Adhesive**

Morrison et al. (2017) provided 12-month outcomes from the VeClose study, a randomized controlled trial in which patients were randomly assigned to receive either endovenous cyanoacrylate closure (CAC; n = 108) or radiofrequency ablation (RFA; n = 114). Of 222 enrolled and randomized subjects, a 12-month follow-up was obtained for 192 (95 CAC and 97 RFA; total follow-up rate, 192/222 [86.5%]). By month 12, the complete occlusion rate was nearly identical in both groups (97.2% in the CAC group and 97.0% in the RFA group). Twelve-month freedom from recanalization was similar in the CAC and RFA groups, although there was a trend toward greater freedom from recanalization in the CAC group (P = .08). The authors reported that symptoms and quality of life improved equally in both groups. Future long-term outcomes are planned.

The VeClose study (Morrison et al., 2015) was a prospective, multicenter randomized controlled U.S. pivotal trial which compared cyanoacrylate adhesive (VenaSeal<sup>®</sup>, Medtronic) to radiofrequency thermal ablation (ClosureFast<sup>®</sup>, Medtronic) for non-inferiority in closure of incompetent great saphenous veins (GSV). Data from this clinical study were the basis for the FDA's pre-market approval (PMA) decision in February 2015. Two hundred twenty-two subjects with symptomatic GSV incompetence were randomly assigned to receive either with VenaSeal or RFA (n = 114) (the first 20 of whom were roll-ins for training of the investigation site personnel and not included in data analysis reports). After discharge, subjects returned to the clinic on day 3 and again at months 1 and 3. The study's primary end point was closure of the target vein at month 3 as assessed by duplex ultrasound and adjudicated by an independent vascular ultrasound core laboratory. Statistical testing focused on showing noninferiority with a 10% delta conditionally followed by superiority testing. No adjunctive procedures such as phlebectomy and US foam sclerotherapy were allowed until after the month 3 visit. Fewer patients required phlebectomy than had been predicted, and fewer than predicted incisions were also required. The 3-month closure rates were 99% for VenaSeal and 96% for RFA. The authors concluded that cyanoacrylate ablation was proven to be noninferior to RFA for the treatment of incompetent GSVs at month 3 after the procedure. Both treatment methods showed good safety profiles. The authors also note that cyanoacrylate ablation does not require tumescent anesthesia and is associated with less

postprocedure ecchymosis. Further studies will be needed to confirm successful closure as well as to demonstrate other advantages of the VenaSeal® procedure, such as lack of necessity for post-procedural compression and any additional benefits of this non-tumescent technique. The study will continue to its three-year conclusion to provide more perspective from longer-term results.

Gibson and Ferris (2017) reported results of the prospective WAVES study of cyanoacrylate closure for the treatment of great saphenous veins, small saphenous veins, and/or accessory saphenous veins up to 20 mm in diameter (n=50). Compression stockings post-procedure were not utilized. Patients returned at 1 week and 1 month for follow-up. All treated veins (48 great saphenous vein, 14 accessory saphenous veins, and 8 small saphenous veins) had complete closure by duplex ultrasound at seven days and one month. Mean time to return to work and normal activities was  $0.2 \pm 1.1$  and  $2.4 \pm 4.1$  days, respectively. The revised venous clinical severity score was improved to  $1.8 \pm 1.4$  ( $p < .001$ ) and Aberdeen Varicose Vein Questionnaire score to  $8.9 \pm 6.6$  ( $p < .001$ ) at one month. Phlebitis in the treatment area or side branches occurred in 10 subjects (20%) and completely resolved in all but one subject (2%) by one month. The authors concluded that cyanoacrylate closure is safe and effective for the treatment of one or more incompetent saphenous or accessory saphenous veins, closure rates were high even in the absence of the use of compression stockings or side branch treatment. Time back to work or normal activities was short and improvements in venous severity scores and QOL were in the authors' opinion significant, comparing favorably with alternative treatment methods. Randomized controlled trials with a larger patient population and longer follow-up periods are needed to validate findings.

Bozkurt and Yilmaz (2016) conducted a prospective comparative study of 310 adult subjects who were treated with cyanoacrylate ablation or endovenous laser ablation. The primary endpoint of this study was complete occlusion of the great saphenous vein. One, three, and 12 months closure rates were 87.1, 91.7, and 92.2% for endovenous laser ablation and 96.7, 96.6, and 95.8% for cyanoacrylate ablation groups. Closure rate at first month was significantly better in cyanoacrylate ablation group ( $<0.001$ ). Although there is a trend of better closure rates in cyanoacrylate ablation patients, this difference did not reach to the statistical difference at sixth and 12th month ( $p = 0.127$  and  $0.138$ , respectively). The authors concluded that the efficacy and safety analysis shows that cyanoacrylate ablation is a safe, simple method which can be recommended as an effective endovenous ablation technique. However, follow-up data of greater than one year is needed to clarify the future role of cyanoacrylate ablation for the treatment incompetent great saphenous veins.

Almeida et al. (2015) evaluated the safety and effectiveness of endovenous cyanoacrylate-based embolization of incompetent great saphenous veins in 38 patients. At 12 months, 36 patients were available for follow-up and 24 patients at 24 months. Complete occlusion of the treated great saphenous vein was confirmed by duplex ultrasound in all patients except for one complete and two partial recanalizations observed at 1, 3 and 6 months of follow-up, respectively. Kaplan-Meier analysis yielded an occlusion rate of 92.0% (95% CI 0.836-1.0) at 24 months follow-up. Venous Clinical Severity Score improved in all patients from a mean of  $6.1 \pm 2.7$  at baseline to  $1.3 \pm 1.1$ ,  $1.5 \pm 1.4$  and  $2.7 \pm 2.5$  at 6, 12 and 24 months, respectively ( $p < .0001$ ). Edema improved in 89% of legs ( $n = 34$ ) at 48 hours follow-up. At baseline, only 13% were free from pain. At 6, 12 and 24 months, 84%, 78% and 64% were free from leg pain, respectively. Small sample size is a limitation to this study.

A prospective multicenter study was conducted on 78 patients with GSV reflux using cyanoacrylate embolization (Proebstle et al., 2015). Clinical examination, quality of life assessment and duplex ultrasound were performed at 2 days, 1, 3, 6, and 12 months. 68 (97.1%) were available for 12-month follow-up. Two-day follow-up showed one proximal and one distal partial recanalization. Three additional proximal recanalizations were observed at 3-month ( $n = 2$ ) and 6-month ( $n = 1$ ) follow-up. Cumulative 12-month survival free from recanalization was 92.9% (95% confidence interval, 87.0%-99.1%). Mean (standard deviation) Venous Clinical Severity Score improved from  $4.3 \pm 2.3$  at baseline to  $1.1 \pm 1.3$  at 12 months. Aberdeen Varicose Vein Questionnaire score showed an improvement from 16.3 at baseline to 6.7 at 12 months ( $P < .0001$ ). Side effects were generally mild; a phlebotic reaction occurred in eight cases (11.4%) with a median duration of 6.5 days (range, 2-12 days). Pain without a phlebotic reaction was observed in five patients (8.6%) for a median duration of 1 day (range, 0 -12 days). No serious adverse event occurred. Paresthesia was not observed. The authors concluded that endovenous CA embolization of refluxing GSVs is safe and effective without the use of tumescent anesthesia or compression stockings. Additional studies are needed to validate the effectiveness of cyanoacrylate embolization.

In a 2015 interventional procedure guideline, the National Institute for Health and Care Excellence (NICE) reports that current evidence on the safety and efficacy of cyanoacrylate glue occlusion for varicose veins is limited in quantity and quality. In addition, as the published evidence is relatively small, rare or uncommon risks may not yet be apparent.

### **Endovenous Foam Sclerotherapy**

Gibson et al. (2017) conducted a randomized, placebo-controlled, multicenter study to evaluate the safety and efficacy of polidocanol endovenous microfoam (1%, Varithena® [polidocanol injectable foam]). Patients ( $n = 77$ ) with symptomatic, visible varicose veins were randomized to treatment with either Varithena 1% or placebo. Patients were

assessed at baseline and weeks 1, 4, 8, and 12 post-treatment. The data showed that Varithena provided greater mean changes from baseline in patient-reported assessments of symptoms (e.g., heaviness, aching, swelling, throbbing, itching [HASTI®] score 30.7 points vs 16.7 points,  $p = 0.0009$ , primary endpoint; and modified Venous Insufficiency Epidemiological and Economic Study-Quality-of-Life/Symptoms [m-VEINES-QOL/Sym;  $p < 0.001$ ]), physician-assessed VCSS, and physician- and patient-assessed appearance compared with placebo. The HASTI score correlated highly with the modified-VEINES-QOL/Sym and Chronic Venous Insufficiency Questionnaire-2 scores ( $r = 0.7$  to  $> 0.9$ ,  $p \leq 0.001$ ). Adverse events included contusion, incision-site hematoma, and limb discomfort. Venous thrombus adverse events were reported as mild and generally resolved without sequelae. Large randomized controlled trials with longer-term outcomes are needed to evaluate the clinical utility of this procedure.

In a multicenter, randomized, placebo-controlled, blinded study in patients with great saphenous vein incompetence and symptomatic and visible superficial venous disease, Vasquez et al. (2017) evaluated the efficacy and safety of polidocanol endovenous microfoam (PEM 0.5%, 1.0%) and placebo each administered with endovenous thermal ablation. Co-primary endpoints were physician-assessed and patient-assessed appearance change from baseline to week 8. A total of 117 patients received treatment (38 placebo, 39 PEM 0.5%, 40 PEM 1%). Physician-rated vein appearance at week 8 was significantly better with PEM ( $p = 0.001$  vs. placebo); patient-assessed appearance trended similarly. In the authors' opinion, polidocanol endovenous microfoam provided improvements in clinically meaningful change in patient-assessed and physician-assessed appearance ( $p < 0.05$ ), need for additional treatment ( $p < 0.05$ ), saphenofemoral junction reflux elimination, symptoms, and QOL. In PEM recipients, the most frequent adverse event was superficial thrombophlebitis (35.4%). A study limitation is short follow-up period for data analysis.

King et al. (2015) designed this pivotal multicenter, parallel group study (VANISH-1), to determine if a single administration of  $\leq 15$  mL of pharmaceutical-grade polidocanol endovenous microfoam (PEM) (Varithena [polidocanol injectable foam]) could alleviate symptoms and improve appearance of varicose veins in a typical population of patients with moderate to very severe symptoms of superficial venous incompetence and visible varicosities of the great saphenous vein (GSV) system. The primary endpoint was patient-reported venous symptom improvement measured by change from baseline to week 8 in 7-day average VVSymQ score. Patients ( $n=279$ ) were randomized to five groups: PEM 0.125% (control), 0.5%, 1%, 2%, or placebo. At week 8, VVSymQ scores for the pooled PEM group (0.5% + 1% + 2%;  $p < .0001$ ) and individual dose concentrations ( $p < .001$ ) were greater as compared to placebo. Most adverse events were mild and resolved without sequelae. No pulmonary emboli were reported. The authors concluded that this study demonstrated that a single administration of up to 15 mL of PEM is a safe, effective, and convenient treatment for the symptoms of superficial venous incompetence and the appearance of visible varicosities of the GSV system. Doses of 0.5%, 1%, and 2% PEM appear to have an acceptable risk-benefit ratio. Additional outcome reporting is planned to evaluate the long-term durability of this procedure.

In the pivotal VANISH-2 trial, Todd et al. (2015) evaluated the efficacy and safety of polidocanol endovenous microfoam in treatment of symptoms and appearance in patients with saphenofemoral junction incompetence due to reflux of the great saphenous vein or major accessory veins. Patients were randomized equally to receive polidocanol endovenous microfoam 0.5%, polidocanol endovenous microfoam 1.0% or placebo. In 232 treated patients, polidocanol endovenous microfoam 0.5% and polidocanol endovenous microfoam 1.0% were superior to placebo, with a larger improvement in symptoms (VVSymQ  $-6.01$  and  $-5.06$ , respectively, versus  $-2.00$ ;  $P < 0.0001$ ) and greater improvements in physician and patient assessments of appearance ( $P < 0.0001$ ). These findings were supported by the results of duplex ultrasound and other clinical measures. Of the 230 polidocanol endovenous microfoam-treated patients (including open-label patients), 60% had an adverse event compared with 39% of placebo; 95% were mild or moderate. The authors concluded that polidocanol endovenous microfoam provided clinically meaningful benefit in treating symptoms and appearance in patients with varicose veins. Longer-term outcomes are needed to evaluate the clinical utility of this procedure.

Lal et al. (2017) evaluated the relationship between patient-reported symptoms and functional and psychological impact of varicose veins following treatment with polidocanol endovenous microfoam (PEM) 1%. Data were pooled from two randomized trials on varicose vein treatment. In 221 patients (109 PEM 1%; 112 placebo), PEM 1% was associated with median improvements of 2.5 points and 4.0 points on the m-VEINES-QOL/Sym functional limitations and m-VEINES-QOL/Sym psychological limitations scores, compared to 0 and 1.0 point. Cumulative distribution function curves revealed that 20-30% more patients in the PEM 1% group achieved clinically meaningful functional and psychological improvement versus placebo group. Patients with above-average symptom improvement had better functional and psychological improvement. PEM 1% treatment had higher odds of clinically meaningful functional and psychological improvement. Length of post-procedure follow-up was not provided.

The National Institute for Health and Care Excellence (NICE) 2013 interventional procedure guidance on ultrasound-guided foam sclerotherapy specifies that if symptoms related to varicose veins are severe, the main treatment options include endovenous laser treatment and radiofrequency ablation, and surgery (ligation and stripping of the great saphenous veins or ligation with or without stripping of the small saphenous veins, and phlebectomy). The NICE 2013

clinical guideline on the diagnosis and treatment of varicose veins adds that if endovenous ablation is unsuitable, offer ultrasound-guided foam sclerotherapy.

### **Professional Societies**

#### ***Society for Vascular Surgery (SVS) / American Venous Forum (AVF)***

The SVS and AVF released joint clinical practice guidelines regarding the care of patients with varicose veins (Gloviczki et al., 2011). The guidelines state that endovenous thermal ablation is recommended over high ligation and inversion stripping of the saphenous vein to the level of the knee. For treatment of the incompetent saphenous vein, the SVS and AVF recommend endovenous thermal ablation over chemical ablation with foam. The guidelines do not discuss MOCA. The policy also states that patients who undergo high ligation alone of the great saphenous vein (GSV) have recurrent reflux in the residual GSV. This causes new symptoms and increases the risk of reoperation.

#### ***American College of Phlebology***

The American College of Phlebology Guidelines Committee (Gibson et al., 2017) performed a systematic review of the literature regarding the clinical impact and treatment of incompetent accessory saphenous veins. They developed a consensus opinion that patients with symptomatic incompetence of the accessory great saphenous veins (anterior and posterior accessory saphenous veins) be treated with endovenous thermal ablation (laser or radiofrequency) or ultrasound-guided foam sclerotherapy to eliminate symptomatology (Recommendation Grade 1C).

The American College of Phlebology Guidelines Committee (2016) updated their evidence-based recommendations for treatment of superficial venous disease of the lower leg. They recommend that named veins (great saphenous vein [GSV], small saphenous vein [SSV], anterior accessory of the great saphenous vein [AAGSV], posterior accessory of the great saphenous vein [PAGSV], intersaphenous vein [Vein of Giacomini]) must have a reflux time > 500 msec regardless of the reported vein diameter (Grade 1A).

Endovenous thermal ablation (laser and radiofrequency) is the Committee's preferred treatment for saphenous and accessory saphenous (GSV, SSV, AAGSV, PAGSV) vein incompetence (Grade 1B). They suggest mechanical/chemical ablation may also be used to treat truncal venous reflux (Grade 2B). They further comment that open surgery is appropriate in veins not amenable to endovenous procedures but otherwise is not recommended because of increased pain, convalescent time, and morbidity (Grade 1B).

### **U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Vein ligation surgery is a procedure and therefore not subject to FDA regulation.

The ClariVein® infusion catheter (Vascular Insights) received FDA approval (K071468) on March 20, 2008. The device is designed to introduce physician-specified medicaments into the peripheral vasculature. See the following website for more information: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf7/K071468.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf7/K071468.pdf). (Accessed January 8, 2018)

The VenaSeal™ Closure System received the FDA's pre-market approval (PMA) on February 20, 2015 (P140018). The device is indicated for the permanent closure of lower extremity superficial truncal veins, such as the great saphenous vein (GSV), through endovascular embolization with coaptation. VenaSeal is intended for use in adults with clinically symptomatic venous reflux as diagnosed by duplex ultrasound (DUS). See the following website for more information: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140018>. (Accessed February 26, 2018)

Varithena (polidocanol injectable foam) (Provensis Ltd.) received FDA approval on November 25, 2013 as a sclerosing agent indicated 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. See the following websites for more information:

- [https://www.accessdata.fda.gov/drugsatfda\\_docs/appletter/2013/205098Orig1s000ltr.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/205098Orig1s000ltr.pdf)
- [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/205098s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/205098s000lbl.pdf)

(Accessed January 8, 2018)

### **CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)**

Medicare does not have a National Coverage Determination (NCD) for surgical and ablative procedures for venous insufficiency and varicose veins. Local Coverage Determinations (LCDs) exist; see the LCDs for [Treatment of Varicose Veins of the Lower Extremity](#), [Varicose Veins of the Lower Extremity](#), [Treatment of](#) and [Treatment of Varicose Veins and Venous Stasis Disease of the Lower Extremities](#).

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#### POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
11/01/2018	<ul style="list-style-type: none"> <li>• Updated coverage rationale; modified language to clarify the listed services are:               <ul style="list-style-type: none"> <li>○ Reconstructive, proven <b>and</b> medically necessary (as described)</li> <li>○ Proven <b>and</b> medically necessary (as described)</li> <li>○ Unproven <b>and</b> not medically necessary (as described)</li> </ul> </li> <li>• Archived previous policy version 2018T0447V</li> </ul>