Surgical and Ablative Procedures for Venous Insufficiency and Varicose Veins (for Louisiana Only)

Policy Number: CS117LA.P~~O~~
Effective Date: ~~April 1, 2020~~**TBD**

➲ Instructions for Use

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Application

This Medical Policy only applies to the state of Louisiana.

Coverage Rationale

➲ See Benefit Considerations

Varicose Vein Ablative and Stripping Procedures

The initial and subsequent radiofrequency ablation, endovenous laser ablation, Stripping, Ligation and excision of the Great Saphenous Vein (GSV) and Small Saphenous Veins (SSV) are considered reconstructive, proven and medically necessary when all of the following criteria are present:

- Junctional Reflux:
  - Ablative therapy for the GSV or SSV only if Junctional Reflux is demonstrated in these veins; or
  - Ablative therapy for Accessory Veins only if anatomically related persistent Junctional Reflux is demonstrated after the GSV or SSV have been removed or ablated
- Individual must have one of the following Functional or Physical 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~~
  - ~~D~~documented Venous Stasis Dermatitis **causing Functional or Physical Impairment**; or
  - Moderate to Severe Pain causing Functional or Physical Impairment.
- Venous Size:
  - The GSV must be 5.5 mm or greater when measured at the proximal thigh immediately below the sapheno~~-~~femoral junction via Duplex Ultrasonography**. (Navarro et al. 2002)**
  - The ~~Small Saphenous Vein~~**SSV** or Accessory Veins must measure 5 mm or greater in diameter immediately below the ~~sapheno-popliteal~~**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 GSV, SSV ~~Veins~~ or principa~~l~~le tributaries.
  - Perforating veins > 350 ms.
  - Some Duplex Ultrasound readings will describe this as moderate to severe reflux which will be acceptable.

~~Refer to the~~**See** Coding Clarification **section**. Adherence to American Medical Association (AMA) coding guidance is required when requesting coverage of endovenous ablation procedures. Note that only one primary code may be requested for the initial vein treated, and only one add-on code per extremity may be requested for any subsequent vein(s) treated.

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 is unproven and not medically necessary due to insufficient evidence of efficacy.

Ligation Procedures

The following procedure is proven and medically necessary:

- Ligation at the saphenofemoral junction, as a stand-alone procedure, 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

The following procedure is proven and medically necessary in certain circumstances:

- **Ligation, subfascial, endoscopic surgery for treatment of perforating veins associated with chronic Venous Insufficiency. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Ligation, Subfascial, Endoscopic, Perforating Vein.**

Click here to view the InterQual® criteria.

The following procedures are unproven and not medically necessary for treating Venous Reflux due to insufficient evidence of efficacy:

- Ligation of the GSV at the saphenofemoral junction, as a stand-alone procedure
- Ligation of the SSV at the saphenopopliteal junction, as a stand-alone procedure
- Ligation at the saphenofemoral junction, as an adjunct to radiofrequency ablation or endovenous laser ablation of the main saphenous veins

Ambulatory Phlebectomy

Ambulatory phlebectomy for treating varicose veins is proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Ambulatory Phlebectomy, Varicose Vein for:

- **Hook Phlebectomy**
- **Microphlebectomy**
- **Mini Phlebectomy**
- **Stab Avulsion**
- **Stab Phlebectomy**

Click here to view the InterQual® criteria.

Other Procedures

The following procedures are unproven and not medically necessary for treating Venous Reflux due to insufficient evidence of efficacy:

- Endovascular embolization of Varicose Veins using cyanoacrylate-based adhesive
- Endovenous low-nitrogen foam sclerotherapy of incompetent GSV, lesser saphenous veins, and accessory saphenous veins.

Definitions

Accessory/Tributary Vein: Axial **a**~~A~~ccessory or ~~T~~**t**ributary ~~S~~**s**aphenous ~~V~~**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.

Cosmetic Procedures: Cosmetic Procedures are excluded from coverage. Procedures or services that change or improve appearance without significantly improving physiological function.

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.

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

Functional or Physical Impairment: A physical or functional 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.

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.

Moderate to Severe Pain: The Venous Clinical Severity Score (VCSS) describes moderate pain to be daily pain or other discomfort interfering with, but not preventing regular daily activities, and severe pain to be daily pain or discomfort that limits most regular daily activities (Vasquez et al. [American Venous Forum], 2010).

Reconstructive Procedures: Reconstructive ~~P~~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 ~~R~~reconstructive ~~P~~procedure.

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

Sclerotherapy: Defined by Watson et al. (2017), sclerotherapy is the intravascular injection of a chemical agent to cause endothelial damage and subsequent vascular occlusion of the target vessel (endovenous chemical ablation).

Sickness: Physical illness, disease or ~~P~~pregnancy. The term Sickness includes ~~M~~mental ~~I~~illness or substance-related and addictive disorders, regardless of the cause or origin of the ~~M~~mental ~~I~~illness or substance-related and addictive disorder.

Small Saphenous Vein: Superficial vein of the calf.

Spider Vein: Spider ~~v~~Veins/~~t~~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 v~~V~~eins: 1 sec
- Superficial ~~V~~veins: 0.5 sec
- Perforator ~~V~~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 federal, state, or contractual requirements 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 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 request treatment of incompetent extremity veins. For sclerosis of veins or endovenous ablation of incompetent extremity veins, see 36468-36479 (CPT Assistant, 2014).
- **Adherence to AMA coding guidance is required when requesting endovenous ablation procedures.**

Per AMA coding guidance, the initial incompetent vein treated (e.g., 36475) may only be requested once per extremity. For endovenous ablation, treatment of subsequent incompetent veins in the same extremity as the initial vein treated (e.g., 36476), only

one add-on code per extremity may be requested, regardless of the number of additional vein(s) treated (CPT Assistant, November 2016).

Therefore, only one primary code may be requested for the initial vein treated, and only one add-on code per extremity may be requested for any subsequent vein(s) treated.

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
***36468**	**Injection(s) of sclerosant for spider veins (telangiectasia), limb or trunk**
****36470**	**Injection of sclerosant; single incompetent vein (other than telangiectasia)**
****36471**	**Injection of sclerosant; multiple incompetent veins (other than telangiectasia), same leg**
36473	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated
36474	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36475	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated
36476	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36478	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated
36479	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36482	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (e.g., cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; first vein treated

CPT Code	Description
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)
37500	**Vascular endoscopy, surgical, with ligation of perforator veins, subfascial (SEPS)**
37700	Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions
37718	Ligation, division, and stripping, short saphenous vein
37722	Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below
37735	**Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia**
37760	**Ligation of perforator veins, subfascial, radical (Linton type), including skin graft, when performed, open,1 leg**
37761	**Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg**
37765	**Stab phlebectomy of varicose veins, one extremity; 10-20 stab incisions**
37766	**Stab phlebectomy of varicose veins, one extremity; more than 20 incisions**
37780	Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)
37785	**Ligation, division, and/or excision of varicose vein cluster(s), one leg**
37799	Unlisted procedure, vascular surgery

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***CPT code 36468 for sclerosant treatment for spider veins is considered cosmetic; does not improve a functional, physical or physiological impairment. (2019 Amendment)**

****CPT codes 36470 and 36471 are covered for sclerotherapy up to 3 sessions per leg within a year. More than 3 sessions per leg within a year is considered cosmetic; does not improve a functional, physical or physiological impairment. (2019 Certificate of Coverage Amendment) Cosmetic sclerotherapy is excluded.**

- **A session is defined as one date of service in which sclerotherapy (36470, 36471) is performed.**
- **A year is defined as a rolling 12 months (365 days).**

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.

Duplex ultrasound is considered the gold standard for diagnosis of superficial venous incompetence. The CEAP (~~C~~**c**linical, ~~E~~**e**tiology, ~~A~~**a**natomy, ~~P~~**p**athophysiology) classification system is used to describe the degree of varicosity. The "C" part of CEAP classification is more useful and practical in rating the severity of Varicose Veins:

- C0: No visible or palpable signs of venous disease
- C1: Telangiectasies (Spider Veins) or Reticular Veins
- C2: Varicose Veins (diameter of vein is > 3mm)
- C3: Edema
- C4a: Pigmentation and eczema
- C4b: Lipodermatosclerosis and atrophie blanche
- C5: Healed venous ulcer
- C6: Active venous ulcer

(**Lurie et al. (**American Venous Forum [AVF]**)**, 20**2**0~~4~~)

Venous clinical severity scoring has been used to measure clinical improvement after treatment of varicose veins. Other venous severity scoring methods include Venous Severity Score, Venous Clinical Severity Score, Venous Segmental Disease Score (**Lurie et al. (**AVF**)**, 20**20**~~18~~).

Preoperative venous duplex ultrasound is used to evaluate patients for venous insufficiency symptoms or suspected DVT; it can provide a road map of vein anatomy similar to contrast venography, as well as essential hemodynamic information about the presence of proximal obstruction, vein valve function, and venous reflux (Lin et al., 2015).

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, 20**20**~~18~~). 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).

Benefit Considerations

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 are 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 ~~above~~.
- Treatments for Spider Veins and/or Telangiectasias are considered to be cosmetic and therefore ~~are~~ excluded from coverage.
- Endovenous Ablation (radiofrequency and/or laser) of either reticular or telangiectatic veins is not reconstructive and not medically necessary and therefore ~~is~~ excluded from coverage.

Sclerotherapy Treatment of Veins

- **Cosmetic sclerotherapy is excluded.**
- **Sclerotherapy up to 3 sessions per leg within a year is covered. More than 3 sessions per leg within a year is considered cosmetic.**
- **A session is defined as one date of service in which sclerotherapy (CPT codes 36470 and 36471) is performed.**
- **A year is defined as a rolling 12 months (365 days).**

Clinical Evidence

A single center randomized controlled trial (RCT) with a follow-up time of 10 years was completed by Eggen et al. (2021) to evaluate the long-term results of saphenofemoral ligation and stripping (SFL/S) compared with 980-nm bare fiber endovenous laser ablation (EVLA) for the treatment of great saphenous vein (GSV) incompetence. Patients with GSV incompetence were randomized to undergo SFL/S or EVLA under tumescent anesthesia. Inclusion criteria were, among others: GSV and SFJ incompetence defined as reflux lasting more than 0.5 seconds on ultrasound imaging after calf compression and release or after the Valsalva maneuver, over an intrafascial length of 15 cm or more measured from the SFJ downward, with a GSV diameter of 3 mm or more or 15 mm or less. The primary outcome was recurrence of groin-related varicose veins seen on duplex ultrasound imaging and clinical examination. The secondary outcomes were (changes or improvement in) CEAP clinical class, venous symptoms, cosmetic results, quality of life, reinterventions, and complications. Between June 2007 and December 2008, 122 patients (130 limbs) were included; of these, 68 limbs were treated with SFL/S and 62 limbs with EVLA. The 10-year estimated freedom from groin recurrence as seen on duplex ultrasound imaging was higher in the SFL/S group (73% vs 44% in the EVLA group; P = .002), and the same trend was seen for clinically evident

recurrence (77% vs 58%, respectively; P = .034). Nine reinterventions (17%) were deemed necessary in the SFL/S group vs 18 (36%) in the EVLA group (P = .059). All re-interventions in the SFL/S group consisted of foam sclerotherapy. Re-interventions in the EVLA group included foam sclerotherapy (n = 5), crossectomy (n = 2), and endovenous procedures (n = 11). There were no significant differences in quality of life and relief of venous symptoms. Cosmetic appearance improved, with a better cosmetic rating in the SFL/S group compared with the EVLA group (P = .026). One patient in the SFL/S group had a persisting neurosensory deficit remaining at 10 years. The authors concluded that the study showed no clear long-term advantage of EVLA with a 980-nm wavelength and bare-tip fiber over high ligation and stripping of the GSV under local tumescent anesthesia.

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 **(RFA)**, 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 ≤ .001. The pooled recurrent reflux rate at the **saphenofemoral junction (**SFJ**)** was significantly lower for HL+S than UGFS (12%, 95% CI 7-20, vs. 29%, 95% CI 21-38; p ≤ .001) and EVLA (12%, 95% CI 7-20, vs. 22%, 95% CI 14-32; p = .038). **Venous Clinical Severity Score (**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. ~~(~~Rass et al. (2015), Gauw et al. (2016), and Flessenkämper et al. (2016), which were previously cited in this policy, are included in ~~the Hamann et al. (2017)~~**this** meta-analysis.~~)~~

Boersma et al. (2016) performed a systematic review and meta-analysis of treatment modalities for small saphenous vein **(SSV)** insufficiency. The review included 49 studies (5 ~~randomized controlled trials~~**RCTs**, 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~~**SSV** 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. ~~(~~Theivacumar et al. (2007) and O'Hare et al. (2008), which were previously cited in this policy, are included in ~~the Boersma et al. (2016)~~**this** meta-analysis.~~)~~

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 SFJ reflux. The occlusion rate was 79.2% at

a mean follow-up of 66.1 months. There were 14 recanalization's and 5 recurrences of the GSV. Five partial and nine total recanalization's 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 and lack of comparison group.

~~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.~~

~~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 controlled trials~~**RCTs** 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~~**RFA**, and five employed ~~endovenous laser ablation~~**EVLA**. 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.

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~~**GSVs**, 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~~**GSV**, reducing postoperative pain and hospital stay.

Woźniak et al. (2016) conducted a ~~quantitative-qualitative analysis~~cohort study 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. The findings are however limited by lack of randomization and a sample size that might have been too small to detect clinically significant differences between the two procedures.**

~~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.~~

Chaar et al. (2011) conducted a retrospective cohort analysis of patients undergoing endovenous laser therapy on the ~~great saphenous vein (~~GSV~~)~~, ~~small saphenous vein (~~SSV~~)~~, or anterior accessory veins (AAV). A total of 732 ablations were reviewed, involving 175 men and 557 women. Veins that measured <1 cm in diameter were considered small, whereas those that measured ≥1 cm at any point were considered to be large. Average follow-up with duplex ultrasound was 3 weeks, and all patients underwent at least one postprocedural ultrasound. In all, 565 (77.3%) GSVs, 113 (15.5%) SSVs, and 53 (7.3%) AAVs were treated. A total of 88 ablations were performed on veins measuring ≥ 1 cm, 12% of all treated veins. In all, 82 GSVs, three SSVs, and three AAVs measured >1 cm, and GSVs comprised 93.2% of treated large veins ($p \leq 0.001$ vs. entire cohort). Based on the results, complication rates and closure rates are not significantly different for veins of diameter ≥ 1 cm and smaller veins. Although more energy is used, the authors observed that this has not translated into higher complication rates, thus in their opinion making EVLT safe and effective for large vein closure. Significantly higher failure and complication rates were seen in SSV and AAV treatment as compared with GSV treatment.

Theivacumar et al. (2011) conducted a cohort study to assess the effectiveness and safety of EVLA in the management of recurrent varicose veins (RVVS). One-hundred four limbs (95 patients) undergoing EVLA for RVVS were grouped according to pattern of reflux. For patients with recurrent SFJ/GSV (Group GR) and SPJ/ SSV (Group SR) varicosities ablation rates and **quality of life (**QoL**) using the** ~~(~~Aberdeen Varicose Vein Severity Scores (AVVSS)~~)~~ were compared with those for age/sex matched patients undergoing EVLA for

primary GSV/SSV dependent varicose veins (Groups GP and SP). In patients with RVVS the axial vein was ablated in 102/104 (98%) limbs while 2 GSVs (group GR) partially recanali~~s~~zed by 3 months (GSV ablated in 49/51 (96%) limbs versus 50/51 (98%) limbs in GP [p = 0.2]). Improvements in AVVSS at 3 months (median GR: 14.2 (inter-quartile range (IQR) 10.2-18.9) to 3.2(1.2-6.4), p < 0.001; GP: median 15.9(IQR 11.4-22.7) to 3.8(1.1-5.6), p < 0.001, Mann-Whitney u-test) were similar (78% versus 76%, p = 0.23). The SSV was ablated in 24/24 limbs in groups SR and SP and the % improvement in AVVSS was 83% (median 14.4 (IQR 8.2-19.4) to 2.4 (1.9-4.6), p < 0.001, Mann-Whitney u-test) and 84% (median 13.8 (IQR 6.3-17.5) to 2.2 (1.2-5.1), p < 0.001) respectively (p = 0.33). These improvements persisted at 1 year follow-up. A further 29 limbs with isolated anterior accessory great saphenous vein (AAGSV) or segmental GSV/SSV reflux were successfully ablated. Complication rates for primary and RVVS were similar. The authors concluded that EVLA is a safe and effective option for the treatment of RVVS and could be a preferred option for suitable patients.

Labropoulos et al. (2010) conducted a prospective study to determine the prevalence, distribution, and extent of varicosities and focal dilatations in the saphenous trunks, their association with the sites of reflux, and their correlation with CEAP classes. Color-flow duplex scan imaging was used to evaluate the entire venous system from groin to ankle for reflux and obstruction. Varicose segments and focal dilatations of the ~~great and small saphenous veins (~~GSV and SSV~~)~~ were recorded, and the diameters throughout the length of the saphenous trunks were measured. The presence of varicosities in the tributaries and accessory veins were documented. The included 500 patients (681 limbs) were divided into two groups based on CEAP class: group A (C2 + C3) and group B (C4-6). Group A had significantly more women than group B and a younger mean age (48 vs 56 years). Overall, GSV reflux (86%) was more prevalent than SSV reflux (17%), P < .0001. Saphenous trunk diameters, ~~saphenofemoral junction (~~SFJ~~)~~ and saphenopopliteal junction (SPJ) involvement were greater in group B, (P < .01). Group C had smaller saphenous diameters compared to group A in all locations (P < .05) but the malleoli. The prevalence of the saphenous varicose segments in both groups was small with the GSV in group B being the highest (4.3%) and the SSV in group A being the smallest (1.2%). Focal dilatations were significantly more prevalent than varicosities in the saphenous trunks (P < .0001). Varicosities of tributaries and accessory veins were more prevalent than those of saphenous trunks (P < .0001). The mean length of varicose segments in the saphenous trunks was short (3.8 cm, range, 2.1-6.4 for group A vs 4.1 cm, range, 2.3-8.3 for group B, P = .09). The authors concluded that focal dilatations are far more common than varicosities. Because both of these entities are more prevalent in the accessory saphenous veins and tributaries, and CEAP class correlates positively with the extent of reflux and saphenous trunk diameter, studies on earlier interventions are warranted to prevent CVD progression.

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~~**GSV**. Similarly, a ~~randomized controlled trial~~**RCT** 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. (2009) compared 33 patients (21 women and 12 men) undergoing ~~anterior accessory great saphenous vein (~~AAGSV~~)~~ EVLA alone (group A) and 33 age/sex-matched

controls undergoing GSV EVLA (Group B) to assess assesses the short-term efficacy (abolition of reflux on Duplex ultrasound) of EVLA of the AAGSV with preservation of a competent GSV in the treatment of varicose veins occurring due to isolated AAGSV incompetence. Comparisons included ultrasound assessment of SFJ competence, successful axial vein ablation, Aberdeen Varicose Vein Symptom Severity Scores (AVVSS) and a visual analogue patient-satisfaction scale. At the 1-year follow-up, EVLA had successfully abolished the target vein reflux ~~+~~(AAGSV: median length 19 cm (inter-quartile range, IQR: 14-24 cm) vs. GSV: 32 cm (IQR 24-42 cm)~~)+~~ and had restored SFJ competence in all patients. Twenty of the 33 patients (61%) in group A and 14 of the 33 (42%) in group B (p=0.218) required post-ablation sclerotherapy at 6 weeks post-procedure for residual varicosities. The AVVSS at 12 months follow-up had improved from the pre-treatment scores in both the groups (group A: median score 4.1 (IQR 2.1-5.2) vs. 11.6 (IQR: 6.9-15.1) p<0.001; group B: median score 3.3 (IQR 1.1-4.5) vs. 14.5 (IQR 7.6-20.2), p<0.001), with no significant difference between the groups. The authors concluded that AAGSV EVLA abolishes SFJ reflux, improves symptom scores and is, therefore, suitable for treating varicose veins associated with AAGSV reflux.

Theivacumar et al. (2008) conducted a randomized controlled trial to assess whether more extensive GSV ablation enhances resolution and influences symptom improvement in patients with previous above-knee (AK) ~~great saphenous vein (~~GSV~~)~~ ~~endovenous laser ablation (~~EVLA~~)~~. Sixty-eight limbs (65 patients) with varicosities and above and below-knee GSV reflux were randomized to Group A: AK-EVLA (n = 23); Group B: EVLA mid-calf to groin (n = 23); and Group C: AK-EVLA, concomitant below-knee GSV foam sclerotherapy (n = 22). Primary outcomes were residual varicosities requiring sclerotherapy (6 weeks), improvement in Aberdeen varicose vein severity scores (AVVSS, 12 weeks), patient satisfaction, and complication rates. EVLA ablated the treated GSV in all limbs. Sclerotherapy requirements were Group A: 14/23 (61%); Group B: 4/23 (17%); and Group C: 8/22 (36%); chi2 = 9.3 (2 df) P = .01 with P(A-B) = 0.006; P(B-C) = 0.19; P(A-C) = 0.14. AVVSS scores improved in all groups as follows: A: 14.8 (9.3-22.6) to 6.4 (3.2-9.1), (P < .001); B: 15.8 (10.2-24.5) to 2.5 (1.1-3.7), (P < .001); and C: 15.1 (9.0-23.1) to 4.1 (2.3-6.8), (P < .001) and P(A-B) = 0.011, P(A -C) = 0.042. Patient satisfaction was highest in Group B. BK-EVLA was not associated with saphenous nerve injury. The authors concluded that extended EVLA is safe, increases spontaneous resolution of varicosities, and has a greater impact on symptom reduction.

Marston et al. (2006) evaluated 89 limbs in 80 patients with CEAP clinical class 3-6 CVI and superficial venous reflux who were treated with saphenous ablation utilizing radiofrequency (RF) or endovenous laser treatment (EVLT). There were no significant differences in preoperative characteristics between the groups treated with RFA or EVLT. Patients were reexamined within 3 months of ablation with duplex to determine anatomic success of the procedure, and with repeat air plethysmography (APG) to determine the degree of hemodynamic improvement. Postoperatively, 86% of limbs demonstrated near total closure of the saphenous vein to within 5 cm of the ~~saphenofemoral junction~~**SFJ**. Eight percent remained open for 5-10 cm from the junction, and 6% demonstrated minimal or no saphenous ablation. The VFI improved significantly after ablation in both the RF and EVLT groups. Post ablation, 78% of the 89 limbs were normal, with a VFI <2 mL/second, and 17% were moderately abnormal, between 2 and 4 mL/second. VCSS scores (11.5 +/-4.5 pre-ablation) decreased significantly after ablation to 4.4 +/-2.3. The authors concluded that minimally invasive saphenous ablation, using either RFA or EVLT, corrects or significantly improved the hemodynamic abnormality and clinical symptoms associated with superficial venous reflux in more than 90% of cases.

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~~**RCTs** 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.

Fifteen hundred consecutive patients were examined by Labropoulos et al. (2004) using duplex ultrasound (DU) to determine the patterns and clinical importance of ~~saphenofemoral junction (~~SFJ~~)~~ reflux in patients with chronic venous disease (CVD) and a normal ~~great saphenous vein (~~GSV~~)~~ trunk~~.~~. Patients with reflux involving the SFJ and/or its tributaries only were included and its prevalence and patterns were studied. Patients with GSV trunk reflux or in any other veins were excluded. The SFJ diameter was categorized as normal, dilated or varicose. The results of surgery were evaluated by DU in 42 patients 1 year after the procedure. SFJ area incompetence with a competent GSV trunk occurred in 8.8% of limbs. It was significantly more common in CEAP class 2, 13.6% compared to class 3, 8.2% (p=0.03), class 1, 2.7%, class 4, 4.4% and classes 5 and 6 together, 1.5% (p<0.001 for all). The SFJ had a normal diameter in 21%, dilated in 62% and varicose in 17%. Reflux was seen in 39% of limbs with a normal SFJ diameter, in 85% of those with a dilated SFJ and in all varicose SFJs. Of the 42 operated limbs, 27 had ligation and division of the SFJ and tributary phlebectomies. Fifteen had tributary phlebectomies only, leaving the SFJ intact. At one-year follow-up, SFJ area reflux was found in six limbs (14.3%), involving the SFJ alone in 1, a main tributary in 1 and 4 small tributaries. No reflux was found in the GSV trunk. All but two of the 42 patients were satisfied with the results. The authors observed that SFJ reflux with tributary involvement and sparing of the GSV trunk occurs in 8.8% of CVD patients. Such reflux is found in the entire spectrum of CVD, but it is more common in class 2. The authors concluded that local surgery with or without SFJ ligation has very good results at 1 year. In addition, they recommend that duplex ultrasound scanning prior to treatment is important in all patients so that the intact GSV can be spared.

In a literature review of long-term results following high ligation supplemented by sclerotherapy, Recek (2004) found that ligation of the ~~saphenofemoral junction~~**SFJ** 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.

In 2004, Winterborn conducted an 11-year follow-up study to a randomized clinical trial (Jones, et al. 1996). The objective of the Jones et al. (1996) trial was to determine whether routine stripping of the long saphenous vein reduced recurrence after varicose vein surgery. Two years after the procedure, 81 patients (113 legs: 53 strip, 60 ligated) with a mean follow-up of 31-months (range 28-33 months) were reassessed with a

satisfaction questionnaire, clinical exam and duplex scanning. Eighty-nine percent were satisfied with their results, although 35% had recurrent veins on clinical examination. Recurrence was reduced from 43% to 25% in patients who had their long saphenous vein stripped (p=0.04). Neovascularis~~z~~zation (serpentine tributaries arising from the ligated ~~saphenofemoral junction~~**SFJ**) was detected in 52% of limbs and was the commonest cause of recurrence. Most tributaries were less than 3 mm in diameter and only caused recurrence if the long saphenous vein or a major thigh vein was intact. Twelve patients had tributaries greater than 3 mm diameter and all had recurrent varicose veins. Winterborn et al. (2004) reported that 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~~**SFJ** 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.

~~Fifteen hundred consecutive patients were examined by Labropoulos et al. (2004) using duplex ultrasound (DU) to determine the patterns and clinical importance of saphenofemoral junction (SFJ) reflux in patients with chronic venous disease (CVD) and a normal great saphenous vein (GSV) trunk.. Patients with reflux involving the SFJ and/or its tributaries only were included and its prevalence and patterns were studied. Patients with GSV trunk reflux or in any other veins were excluded. The SFJ diameter was categorized as normal, dilated or varicose. The results of surgery were evaluated by DU in 42 patients 1 year after the procedure. SFJ area incompetence with a competent GSV trunk occurred in 8.8% of limbs. It was significantly more common in CEAP class 2, 13.6% compared to class 3, 8.2% (p=0.03), class 1, 2.7%, class 4, 4.4% and classes 5 and 6 together, 1.5% (p<0.001 for all). The SFJ had a normal diameter in 21%, dilated in 62% and varicose in 17%. Reflux was seen in 39% of limbs with a normal SFJ diameter, in 85% of those with a dilated SFJ and in all varicose SFJs. Of the 42 operated limbs, 27 had ligation and division of the SFJ and tributary phlebectomies. Fifteen had tributary phlebectomies only, leaving the SFJ intact. At one year follow up, SFJ area reflux was found in six limbs (14.3%), involving the SFJ alone in 1, a main tributary in 1 and 4 small tributaries. No reflux was found in the GSV trunk. All but two of the 42 patients were satisfied with the results. The authors observed that SFJ reflux with tributary involvement and sparing of the GSV trunk occurs in 8.8% of CVD patients. Such reflux is found in the entire spectrum of CVD, but it is more common in class 2. The authors concluded that local surgery with or without SFJ ligation has very good results at 1 year. In addition, they recommend that duplex ultrasound scanning prior to treatment is important in all patients so that the intact GSV can be spared.~~

~~Probstle et al. (2003) studied 85 consecutive patients with clinical stage C(2-6) E(P,S) A(S,P,D) P(R) disease to establish the incidence of early recanalization after endovenous laser treatment (ELT) and evaluate the histopathologic features of reperfused and excised GSV. Twelve months of follow-up with duplex scanning at regular intervals was possible in 104 treated veins (95.4%) in 82 patients (96.5%). Recanalized vessels were removed surgically and examined at histopathology. ELT-induced occlusion proved permanent at duplex scanning over 12 months of follow-up in 94 of 104 GSV (90.4%) in 73 patients. In 4~~

~~patients, 5 GSV (4.8%) were recanalized completely after 1 week, after 3 months (n=3), or after 12 months. Another 5 GSV (4.8%) in 5 patients exhibited incomplete proximal recanalization over the 12 months of follow-up. Finally, 9 recanalized vessels (8.6%) required further treatment with high ligation and stripping. The authors concluded that early recanalization requiring retreatment is observed in less than 10% of GSV after ELT. The histopathologic pattern mimics recanalization after thrombophlebotic occlusion.~~

Labropoulos et al. (2003) conducted a prospective study to determine the upper limits of normal for duration and maximum velocity of retrograde flow (RF) in lower extremity veins. Eighty limbs in 40 healthy subjects and 60 limbs in 45 patients with chronic venous disease were examined with duplex scanning in the standing and supine positions. Each limb was assessed for reflux at 16 venous sites, including the common femoral, deep femoral, and proximal and distal femoral veins; proximal and distal popliteal veins; gastrocnemial vein; anterior and posterior tibial veins; peroneal vein; ~~greater saphenous vein~~**GSV**, at the ~~saphenofemoral junction~~**SFJ**, thigh, upper calf, and lower calf; and lesser saphenous vein, at the ~~saphenopopliteal junction~~**SPJ** and mid-calf. Perforator veins along the course of these veins were also assessed. In the healthy volunteers, 1553 vein segments were assessed, including 480 superficial vein segments, 800 deep vein segments, and 273 perforator vein segments; and in the patients, 1272 vein segments were assessed, including 360 superficial vein segments, 600 deep vein segments, and 312 perforator vein segments. Detection and measurement of reflux were performed at duplex scanning. Standard pneumatic cuff compression pressure was used to elicit reflux. Duration of RF and peak vein velocity were measured immediately after release of compression. Based on the results, the authors observed that the cutoff value for reflux in the superficial and deep calf veins is greater than 500 ms. However, in their opinion the reflux cutoff value for the femoropopliteal veins should be greater than 1000 ms. Outward flow in the perforating veins should be considered abnormal at greater than 350 ms. Reflux testing should be performed with the patient standing.

Proebstle et al. (2003) studied 85 consecutive patients with clinical stage C(2-6) E(P,S) A(S,P,D) P(R) disease to establish the incidence of early recanalization after endovenous laser treatment (ELT) and evaluate the histopathologic features of reperfused and excised GSV. Twelve months of follow-up with duplex scanning at regular intervals was possible in 104 treated veins (95.4%) in 82 patients (96.5%). Recanalized vessels were removed surgically and examined at histopathology. ELT-induced occlusion proved permanent at duplex scanning over 12 months of follow-up in 94 of 104 GSV (90.4%) in 73 patients. In 4 patients, 5 GSV (4.8%) were recanalized completely after 1 week, after 3 months (n=3), or after 12 months. Another 5 GSV (4.8%) in 5 patients exhibited incomplete proximal recanalization over the 12 months of follow-up. Finally, 9 recanalized vessels (8.6%) required further treatment with high ligation and stripping. The authors concluded that early recanalization requiring retreatment is observed in less than 10% of GSV after ELT. The histopathologic pattern mimics recanalization after thrombophlebotic occlusion.

In a cohort study, Navarro et al. (2002) evaluated the clinical significance of GSV diameter determined in the thigh and calf as a marker of global hemodynamic impairment and clinical severity in a model comprising patients with ~~saphenofemoral junction~~**SFJ** and truncal GSV incompetence. Eighty-five consecutive patients, aged 28 to 82 (mean, 46.2) years; 112 lower limbs with ~~saphenofemoral junction~~**SFJ** and truncal GSV incompetence were investigated. The GSV diameter was measured on standing at the knee, and at 10, 20, and 30 cm above and below the knee, and in the thigh and calf, respectively, using B-mode imaging. The venous filling index (VFI), venous volume (VV), and residual volume fraction (RVF) were measured by air plethysmography. The GSV diameter at all 7 limb levels studied

correlated well with VV (except at the distal calf), VFI, RVF, and CEAP (P< or =.009 for all). A GSV diameter of 5.5 mm or less predicted the absence of abnormal reflux, with a sensitivity of 78%, a specificity of 87%, positive and negative predictive values of 78%, and an accuracy of 82%. A GSV diameter of 7.3 mm or greater predicted critical reflux (VFI >7 mL/s), with an 80% sensitivity, an 85% specificity, and an 84% accuracy. In the authors' opinion, GSV diameter proved to be a relatively accurate measure of hemodynamic impairment and clinical severity in a model of ~~saphenofemoral junction~~**SFJ** and GSV incompetence, predicting not only the absence of abnormal reflux, but also the presence of critical venous incompetence, assisting in clinical decision making before considering greater saphenectomy.

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~~**SFJ** and reduce the incidence of PE. The two types of surgical treatment were ligation of the ~~great saphenous vein~~**GSV** at the ~~saphenofemoral junction~~**SFJ** 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~~**DVT** and ~~pulmonary embolism~~**PE** development as compared to surgical treatment with ligation of the ~~great saphenous vein~~**GSV** at the ~~saphenofemoral junction~~**SFJ** or ligation and stripping.

Chandler et al. (2000) conducted a prospective, comparative study to evaluate the effect of extended ~~saphenofemoral junction (~~SFJ~~)~~ ligation when the ~~greater saphenous vein (~~GSV~~)~~ has been eliminated from participating in thigh reflux by means of endovenous obliteration. Sixty limbs treated with SFJ ligation and 120 limbs treated without high ligation were selected from an ongoing, multicenter, endovenous obliteration trial on the basis of their having primary varicose veins, GSV reflux, and early treatment dates. Five (8%) high-ligation limbs and seven (6%) limbs without high ligation with patent veins at 6 weeks or less were excluded as unsuccessful obliterations. Treatment significantly reduced symptoms and CEAP clinical class in both groups (P =.0001). Recurrent reflux developed in one (2%) of 49 high-ligation limbs and eight (8%) of 97 limbs without high ligation by 6 months (P =.273). New instances of reflux did not appear thereafter in 57 limbs followed to 12 months. Recurrent varicose veins occurred in three high-ligation limbs and four limbs without high ligation by 6 months and in one additional high-ligation limb and two additional limbs without high ligation by 12 months. Actuarial recurrence curves were not statistically different with or without SFJ ligation (P >.156), predicting greater than 90% freedom from recurrent reflux and varicosities at 1 year for both groups. According to the authors, these early results suggest that extended SFJ ligation may add little to effective GSV obliteration, but their findings are not sufficiently robust to warrant abandonment of SFJ ligation as currently practiced in the management of primary varicose veins associated with GSV vein reflux.

Labropoulos et al. (1999) studied the distribution and extent of non-truncal superficial venous reflux and its association with the signs and symptoms of chronic venous disease (CVD) in eighty-four limbs in 62 patients with signs and symptoms of CVD and evidence of

reflux on continuous-wave Doppler. Incompetent superficial vein tributaries were imaged throughout their extent and both ends were identified. Limbs with reflux in the main trunk of the saphenous veins or the deep, perforator or muscular veins, superficial or deep vein thrombosis, injection sclerotherapy, varicose-vein surgery, arterial disease and inflammation of non-venous origin were excluded from the study. The authors observed that this data indicate that reflux confined to superficial tributaries is found throughout the lower limb. Because this reflux is present without greater and lesser saphenous trunk, perforator and deep-vein incompetence or proximal obstruction, it shows that reflux can develop in any vein without an apparent feeding source. Greater saphenous tributaries are affected significantly more often than those of lesser saphenous, while non-saphenous reflux is uncommon. Most limbs have signs and symptoms of CVD class 2 and 15% belong in classes 3 and 4.

Endovenous Mechanochemical Ablation

Evidence in peer review literature evaluating endovenous mechanochemical ablation (MOCA) for the treatment of venous insufficiency and varicose veins is limited. Future robust RCTs are warranted along with long-term outcomes to establish the safety and efficacy of this procedure.

Mohamed et al. (2021) conducted a single-center RCT to compare the technical, clinical and QOL outcomes after EVLA and MOCA. One hundred fifty patients with symptomatic, unilateral, single-axis superficial venous incompetence (SVI) were randomized equally to either EVLA or MOCA, both with concomitant phlebectomy when necessary. Primary outcomes were intraprocedural axial ablation pain scores and anatomical occlusion at 1 year. Secondary outcomes included postprocedural pain, VCSS, QoL (Aberdeen Varicose Veins Questionnaire (AVVQ) and EuroQol 5-domain utility index), patient satisfaction and complication rates. Both groups reported low intraprocedural pain scores; on a 100 mm visual analog scale, pain during axial EVLA was 22 (9-44) compared to 15 (9-29) during MOCA. At 1-year, duplex derived anatomical occlusion rates after EVLA were 63/69 (91%) compared to 53/69 (77%) in the MOCA group (p=0.02). Both groups experienced improvement in VCSS and AVVQ after treatment, without a significant difference between groups. Median VCSS improved from 6 (5-8) to 0 (0-1) at one year. Median AVVQ improved from 13.8 (10.0-17.7) to 2.0 (0.0-4.9). One patient in the MOCA group experienced DVT. The authors concluded EVLA resulted in a higher technical success rate compared to MOCA but clinically, both treatments were highly efficacious in treating SVI. Patients improved in terms of symptoms, disease severity and QoL. Both procedures resulted in low procedural pain with a short recovery time. EVLA had higher axial occlusion rates. The authors noted that higher recanalization rates after MOCA may lead to higher rates of recurrence and long-term follow-up is needed. Long-term follow up at 5 and 10 years is planned for this study. Limitations include short term follow up and single-center recruitment.

In an updated Cochrane review, Whing et al. (2021) compared interventions for treating varicosities of the GSV. The review included 24 RCTs with 5135 participants who underwent EVLA, RFA, EVSA, UGFS, cyanoacrylate glue, MOCA, or high ligation and stripping. The authors found there was no clear difference in technical success or recurrence between RFA compared to MCOA, however, long-term data were not available, and the confidence intervals of the combined data were broad, making these findings largely inconclusive. Additionally, the authors noted all the trials had some risk of bias concerns. The authors determined there were a relatively small number of studies for comparison and differences in outcome definitions and time points reported limited their conclusions. Future studies which provide more evidence on the breadth of treatments are recommended

by the authors. Bootun et al. (2016), Lane et al. (2017), Holewijn et al. (2019), Vähäaho et al. (2019), which were previously cited in this policy, are included in this review. ~~Holewijn et al. (2019) conducted a multi-center, randomized controlled trial comparing mechanical occlusion chemically assisted endovenous ablation (MOCA) and radiofrequency ablation (RFA) in the treatment of primary great saphenous vein incompetence. The primary endpoints were pain at 2 weeks after treatment and anatomic success at 1 year after treatment. Secondary endpoints included disease-specific and general health-related quality of life (HRQoL). Sample size calculations were performed and target enrollment was set at 230 patients in each arm (assumed 10% lost to follow-up; α, 5%; power, 80%). A total of 209 patients were treated (105 in the MOCA group and 104 in the RFA group). During the 14 days after treatment, median pain scores were lower in the MOCA group compared with the RFA group (0.2 vs 0.5 p=0.010). At 30 days after treatment, similar complication numbers (MOCA, n=62; RFA, n=63) and HRQoL scores (Aberdeen Varicose Vein Questionnaire: MOCA, 8.9; RFA, 7.6; p=0.233) were observed. Hyperpigmentation was reported in seven patients in the MOCA group and in two patients in the RFA group (p=0.038). The MOCA group had four complete failures (3.8%) compared with none in the RFA group (p=0.045). Median 30-day Venous Clinical Severity Score (VCSS) was significantly lower at 30 days after MOCA vs. RFA (1.0 vs 2.0 p=0.001), although VCSS was comparable at baseline. The 1- and 2- year anatomic success rates were lower after MOCA (83.5% and 80.0%) compared with RFA (94.2% and 88.3%; p=0.025 and 0.066). After 2 years of follow-up, no differences were observed in the number of complete failures. At 1 year and 2 years after treatment, there were no differences in clinical success rates or HRQoL scores between the treatment groups. There were two patients with cardiac events: ventricular fibrillation (1 year, MOCA) and unstable angina (2 years, RFA), and one patient with a deep venous thrombosis (1 year, RFA). The authors concluded that in the short term, unilateral treatment with MOCA resulted in less postoperative pain but more hyperpigmentation compared with RFA, and there were more anatomic failures reported after MOCA, but both techniques were associated with similar clinical outcomes at 1 year and 2 years after treatment. Study limitations include: 1) that the study failed to reach its targeted number of participants as it was terminated early; 2) not all questionnaires were fully completed; and 3) the use of self-reported data, which may contain sources of bias.~~

~~Vähäaho et al. (2019) conducted a single-center, randomized controlled trial to evaluate great saphenous vein occlusion (GSV) rates among patients who underwent mechanical occlusion chemically assisted endovenous ablation (MOCA), thermal ablation with endovenous laser (EVLA) or radiofrequency ablation (RFA). The primary outcome was GSV occlusion rate at 1-year and secondary outcomes were quality of life, patient-reported pain during and after treatment, duration of sick leave, and 30-day complications. Target enrollment was set at 160 patients (assumed 5% lost to follow-up) to detect a 20% difference in occluded or absent GSV between the MOCA and thermal ablation groups (α, 5%; power, 80%). A total of 132 patients participated in the study and the final analytic sample consisted of 117 patients: 55 patients who were randomized to MOCA, 33 to EVLA and 29 to RFA. During the procedure, if patients experienced pain, they were given propofol or fentanyl. At 1-year after treatment, the GSV occlusion rates were 100% for the EVLA and RFA groups and 82% for the MOCA group (p=0.002). Ten patients in the MOCA group had recanalization in the treated GSV. During the procedure, before discharge and at 1 week after treatment, mean pain scores were similar across the groups (p=0.118, p=0.176 and p=0.915, respectively). At 1-month after treatment, all treated GSVs were occluded regardless of treatment method. One patient in the MOCA group had a superficial infection that was treated with oral antibiotics. There were no DVT cases or differences in the frequency of hematomas, pigmentation or palpable lumps between the groups. Duration of~~

~~sick leave did not differ between the groups (p=0.841). At 1-year after treatment, QOL had improved compared to baseline in all groups, and there were no significant differences between the groups. The authors concluded that the 1-year GSV occlusion rate for EVLA and RFA were higher than MOCA, while QOL was similar between the treatment methods. Study limitations include: 1) that the study failed to reach its targeted number of participants; 2) patients, surgeons and follow-up assessors were not blinded to the type of treatment that was given; and 3) medications given during treatment or concomitant phlebectomies may have affected the reliability of the pain scores.~~

Kim et al. (2017) evaluated in a case series whether early efficacy in endovenous ~~mechanochemical ablation (~~MOCA~~)~~ is maintained at 24 months. Patients with reflux in the ~~great saphenous vein~~GSV 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~~VCSS. 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 ± 14 years and an average BMI of 30.5 ± 6. The mean ~~great saphenous vein~~GSV 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~~VCSS (P < .001) for all time intervals. Early high occlusion rate with ~~mechanochemical ablation~~MOCA is associated with significant clinical improvement, which ~~is~~was maintained at 24 months.~~, which a~~ According to the authors, this finding is suggestive of a good option for the treatment of ~~great saphenous vein~~GSV incompetence. Longer-term outcomes are needed to evaluate MOCA's efficacy. The study is limited by lack of comparison group and large loss to follow-up.

Vos et al. (2017) conducted a systematic review and meta-analysis to evaluate the efficacy of ~~mechanochemical endovenous ablation (~~MOCA~~)~~ and cyanoacrylate vein ablation (CAVA) for GSV incompetence. Eligible articles were prospective studies that included patients treated for GSV incompetence and described the primary outcome. Exclusion criteria were full text not available, case reports, retrospective studies, small series (n < 10), reviews, abstracts, animal studies, studies of ~~small saphenous vein~~SSV incompetence, and recurrent GSV incompetence. Primary outcome was anatomic success. Secondary outcomes were initial technical success, ~~Venous Clinical Severity Score~~VCSS, ~~Aberdeen Varicose Vein Questionnaire~~AVVQ score, and complications. Fifteen articles met the inclusion criteria. Pooled anatomic success for MOCA and CAVA was 94.7% and 94.8% at 6 months and 94.1% and 89.0% at 1~~-~~-year, respectively. ~~Venous Clinical Severity Score~~VCSS and ~~Aberdeen Varicose Vein Questionnaire~~AVVQ score significantly improved after treatment with MOCA and CAVA. The authors conclude that both of these non-thermal techniques are promising that could serve as alternatives for thermal ablation techniques. However, to determine their exact role in clinical practice, high-quality ~~randomized controlled trials~~RCTs comparing these novel modalities with well-established techniques are required. **This study is limited by inclusion or mostly uncontrolled studies to assess the efficacy and safety of MOCA.** ~~(~~Elias and Raines (2012) and Bishawi et al. (2014), which were previously cited in this policy, are included in ~~the Vos et al. (2017)~~**this** meta-analysis.~~)~~

Witte et al. (2017a) conducted a systematic review and meta-analysis of MOCA of saphenous veins using the ClariVein to report on the anatomical, technical, and clinical success. The literature search identified 759 records, of which 13 were included, describing 10 unique cohorts. A total of 1521 veins (1267 ~~great saphenous vein~~**GSV** and 254 ~~small saphenous vein~~**SSV**) were included, with cohort sizes ranging from 30 to 570 veins. The pooled anatomical success rate after short-term follow up was 92% (95% CI 90-94%) (n=1314 veins). After 6 and 12 months these numbers were 92% (95% CI 88-95%) (n=284) and 91% (95% CI 86-94%) (n=228), respectively. The long-term anatomical success rates at 2 and 3 years were 91% (95% CI 85-95%) (n=136) and 87% (95% CI 75-94%) (n=48), respectively. Major complications and especially nerve injury were very rare (≤ 0.2%). All studies were of moderate or good quality using the **methodological index for non-randomized studies (**MINORS**)** scoring scale. The authors concluded that MOCA using the ClariVein in combination with liquid sclerosant is associated with an anatomical success rate ranging from 87% to 92% and good clinical success. However, they reported that no ~~randomized controlled trials~~**RCTs** are available studying the anatomical success after MOCA compared to the endothermal 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 ± 14 years and an average BMI of 30.5 ± 6. The mean great saphenous vein diameter in the upper thigh was 7.6mm 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**b**) 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~~**QoL** 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 preprocedur~~e~~**al** 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~~**QoL**. 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. **Additionally, these findings are limited by lack of comparison group undergoing a different treatment.**

~~Lane et al. (2016) conducted a multi-center, randomized controlled trial to evaluate pain associated with mechanical occlusion chemically assisted endovenous ablation (MOCA) versus radiofrequency endovenous ablation (RFA). Patients with great saphenous vein (GSV) or small saphenous vein (SSV) incompetence were randomized to receive MOCA or RFA. Those with recurrent varicose veins, current deep vein thrombosis, arterial disease, veins less than 3mm in diameter, or hypercoagulability were excluded. The primary outcome, patient-reported pain during ablation, was assessed using a Visual Analog Scale (VAS, 1-10). Secondary outcomes included patient-reported quality of life (disease-specific and generic) and clinical severity scores at months 1 and 6 after ablation, and time to return to normal activities and work. At total of 170 patients participated, 87 patients underwent MOCA and 83 underwent RFA. The maximum pain experienced during the procedure was lower in the MOCA group than the RFA group (15 mm vs. 34 mm, p=0.003, respectively). At month 1 and month 6, there were no differences in disease-specific QOL, generic QOL, or clinical severity scores between the MOCA and RFA groups. There was no difference between the groups for time required to return to work or normal activities, with a median of 2 days for each group. There was no difference in occlusion rates at 1 month or 6 months between the groups (p=0.403 and p=0.483, respectively). The authors concluded that MOCA offers patients reduced intra-procedural pain with short-term outcomes similar to RFA, and that larger studies with longer follow-up are needed. Study limitations include: 1) the lack of blinding, which could lead to information bias with respect to patients self-reported pain levels; 2) the primary outcome was an assessment of pain during the procedure and that pain was not assessed after the procedure or after phlebectomy; and 3) the short follow-up period.~~

~~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.~~

Vun et al. (2015) assessed the efficacy of the ClariVein system for the treatment of superficial vein incompetence. Fifty-one ~~great saphenous veins~~**GSVs** and six ~~small saphenous veins~~**SSVs** 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 ~~cohort study~~case series, 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~~ **group, small sample size and short-term follow-up.**

In a prospective comparison study, van Eekeren et al. (2013) evaluated postoperative pain and ~~quality of life~~**QoL** 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~~**QoL**. 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.~~

In a pilot study, ~~V~~**v**an 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® 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. **This study is limited by lack of comparison group undergoing a different treatment approach.**

~~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

Quality evidence in peer review literature evaluating endovascular embolization with cyanoacrylate-based adhesive for the treatment of venous insufficiency and varicose veins is limited. Future robust RCTs are warranted along with long-term outcomes to establish

the safety and efficacy of this procedure. An ongoing RCT may provide more definitive findings about this technology (NCT03820947).

An ECRI clinical evidence assessment (2021) suggests that VenaSeal is safe and as effective as RFA for treating varicose veins in patients with venous reflux disease. However, how well VenaSeal works compared with other treatment modalities cannot be determined because the SR assessed too few patients for each comparison and no studies in the SR performed head-to-head comparisons. The report determined the evidence was somewhat favorable but RCTs are needed to compare VenaSeal with other treatment modalities. Limitations of the reviewed studies include risk for lack of blinding, single-center focus, and lack of randomization.

A Hayes report, Cyanoacrylate Embolization (VenaSeal Closure System) for the Treatment of Varicose Veins, evaluated 7 clinical studies on the efficacy and safety of cyanoacrylate embolization with the VenaSeal Closure System. The evidence included 1 randomized controlled trial, 1 cohort study, 1 case series and 4 pre-post studies. The conclusion states that this **approach has potential but unproven benefits and that a** low-quality body of evidence suggests that the VenaSeal Closure System may result in reduced symptom severity, improved **QoL** ~~quality of life~~ and similar occlusion rates when compared with ~~radiofrequency ablation~~**RFA** however, substantial uncertainly remains regarding its effectiveness due to the lack of well-designed comparative studies (20**20**~~19~~**, updated 2021**).

~~An ECRI Health Technology Assessment on the VenaSeal Closure System reviewed 5 studies. One randomized controlled trial and 1 nonrandomized comparative study showed that the VenaSeal is as safe and effective as radiofrequency ablation in achieving vein closure, resolving symptoms and improving quality of life. Three additional case series showed high vein closure success. However, the report states that additional randomized controlled trials comparing VenaSeal with other treatment modalities and reporting on longer-term follow-up are needed (2019).~~

Joh et al. (2021) conducted an open-label multicenter, prospective, randomized controlled trial that compare the clinical outcomes of cyanoacrylate closure (CAC) and surgical stripping (SS) for the treatment of incompetent great saphenous veins. One hundred and twenty-six patients were randomized into two groups (63 with CAC and 63 with SS). Target vein occlusion was assessed on the third day and 1, 3, 6, and 12 months postoperatively using duplex ultrasound. The primary endpoint of the study was to evaluate complete closure of the target vein at 3 months. Ecchymosis grades, VCSS, AVVQ score and pain were also assessed as secondary outcomes. Postoperative pain scores were significantly better in the CAC group than in the SS group. In addition, the mean ecchymosis grade was 0.3 ± 0.5 in the CAC group and 1.1 ± 1.1 in the SS group (P < .001). The VCSS and QoL had improved equally in both groups. Most complications were minor (9 events in CAC group and 20 events in SS group) with one major complication occurring in a patient who had undergone the SS procedure. Complete occlusion of the target vein at 3 months was achieved by both procedures. Postoperative pain and ecchymosis grades were significantly lower in the CAC group. The authors concluded that CAC has a high success rate with few complications. Limitations noted by the authors include lack of information on patient return to work and daily activities, pain scores during the procedure and immediately after the procedure were not obtained, the 2X2 factorial design with 1:1 randomization, could contribute to differences in gender distribution and VCSSs in the two groups and concomitant phlebectomy could have also influenced the occurrence of complications. Additionally, lack of masking could have introduced a bias in the findings.

The VenaSeal Sapheon Closure System Pivotal Study (VeClose) is a multi-center RCT that compared cyanoacrylate closure CAC to RFA for the treatment of incompetent great saphenous veins. In this trial, 222 subjects with symptomatic GSV incompetence were randomly assigned to receive either CAC (n=108) with the VenaSeal Sapheon Closure System or RFA (n=114). The primary endpoint was closure of the target vein at month 3, as assessed by duplex ultrasound. To determine non-inferiority of CAE to RFA, the investigators used a predetermined margin of 10%. Secondary endpoints included subject-rated pain experienced during the procedure (i.e., pain experienced after vein access but before all treatment/access catheters were removed), investigator-rated ecchymosis at day 3, adverse events, and details of adjunctive procedures. Patient follow-up visits were on day 3 and at months 1, 3, 6, 12, 24, and 36. For the extension study, patients who were successfully contacted and were interested in participation provided written informed consent for the 60-month follow-up visit. Assessments tools included the VCSS, AVVQ and EuroQol-Five Dimension (EQ-5D) quality of life survey. This trial has generated multiple publications that reported outcomes with various follow-up periods e.g., 3 months (Morrison, 2015), 12 months (Morrison, 2017) 24 months (Gibson, 2018a) 36 months (Morrison, 2019), and 60 months (Morrison, 2020), as well as a publication with results of a roll-in phase analysis, which included 20 additional patients treated with CAC (Kolluri, 2016). Design limitations of this study and the resulting publications included lack of blinding of the subjects or assessors to the intervention. Furthermore, the primary endpoint of the study was complete closure of the target vein at 3 months after index treatment, thus the study may not have been powered to detect clinically significant differences between treatments groups for important outcomes and at different times of follow-up. These studies were also included in the Hayes report (2020; updated 2021). The individual studies are listed below:

- Morrison et al. (2015) reported 3-month outcomes from the VeClose trial. No adjunctive procedures such as phlebectomy and UGFS were allowed until after the month 3 visit. The closure rates were 99% for VenaSeal and 96% for RFA. Pain experienced during the procedure was reported as mild and was similar between treatment groups. Good safety profiles were reported with both treatments. The authors concluded that cyanoacrylate ablation did not require tumescent anesthesia, was associated with less post procedure ecchymosis, and was noninferior to RFA for the treatment of incompetent GSVs at month 3 after the procedure.
- Morrison et al. (2017) reported 12-month outcomes from the VeClose trial. Of 222 randomized patients, a 12-month follow-up was obtained for 192 (95 CAC and 97 RFA; total follow-up rate, 86.5%). 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 patient symptoms and QoL improved equally in both groups.
- Twenty-four-month outcomes from the VeClose trial were reported by Gibson et al (2018a). One hundred and seventy-one patients completed the 24-month follow-up, which included 87 from the CAC group and 84 from the RFA group. The 24-month GSV closure rate was 95.3% in the CAC group and 94.0% in the RFA group. Symptoms and QoL improved similarly in both groups. No clinically significant device- or procedure-related late adverse events were reported. The authors concluded that both CAC and RFA were effective in closure of the target GSV, resulting in similar and significant improvements in the patient's QoL through 24 months.
- One hundred and forty-six patients completed the 36-month follow-up to the VeClose trial, which included 72 patients from the CAC group and 74 patients from the RFA

group, with outcomes reported by Morrison et al. (2019). The 36-month GSV closure rate was 94.4% for the CAC group and 91.9% for the RFA group. Stable improvement in symptoms and QoL was observed in both groups. Adverse event rates between the 24- and 36-month visits were similar between the groups as were serious adverse events which were infrequent and judged unrelated to either the device or the procedure in both groups. The authors surmised the results of this trial continue to demonstrate the safety and efficacy of CAC for the treatment of GSV incompetence with vein closure rate at 36 months similar to that of RFA. The findings are limited by the loss to follow up (34%), which could have introduced biases in the findings.

- Morrison et. al. (2020) reported 60-month outcomes from the VeClose trial with a total of 89 patients in the original study completing the 60-month visit. Of those, 47 patients were from the CAC group, 33 patients were from the RFA group, and 9 patients were from the roll-in CAC group. No new recanalization events were observed between 36 and 60 months of follow-up. Kaplan-Meier estimates for freedom from recanalization in the randomized CAC and RFA groups were 91.4% and 85.2%, respectively. Both groups demonstrated sustained improvements in EuroQol-5 Dimension (EQ-5D) and QoL. Whereas patients assigned to C0 or C1 clinical class were excluded from the original study, more than half of all returning patients (64% [57/89]) were now assigned to C0 or C1, suggesting an improved clinical class from baseline. Furthermore, 41.1% of returning CAC patients and 39.4% of returning RFA patients at least two CEAP clinical classes lower than at baseline. The authors concluded that CAC and RFA were effective in achieving complete target vein closure of the GSV at long-term follow-up. CAC was also associated with sustained improvements in symptoms and QoL, lower CEAP class, and high level of patient satisfaction without serious adverse effects between 36 and 60 months. The limitations of this publication included the small rate of successful follow up i.e., 36% of the original study randomized population, which could have introduced biases in the findings.

A systematic review by Dimech and Cassar (2020) was performed to assess the efficacy of *n*-butyl-2-cyanoacrylate (NBCA) glue in ablating primary truncal varicose veins and eliminating reflux compared with existing endovascular techniques. Secondary outcomes include complications and quality of life. PRISMA was used as a guide, and studies were screened for risk of bias and methodological quality. Subjects had to be ≥18 years of age and followed-up post-treatment with color Duplex ultrasound (DUS). Eligibility criteria included saphenofemoral junction (SFJ) or saphenopopliteal junction (SPJ) incompetence with reflux down truncal veins lasting >0.5 seconds on DUS interrogation and a Clinical, Etiological, Anatomical, and Pathophysiological classification of venous disorders ranging between C1 and C6. Out of 2,910 patients (3,220 veins) in 17 studies, 1,981 were administered NBCA, 445 radiofrequency ablation (RFA), and 484 endovenous laser ablation (EVLA) with mean procedure times of 25.7, 23.2, and 28.7 minutes, respectively. Mean recruitment period was 9 months (1-36 months) and followed-up for an average of 12.3 months (1-36 months). The majority were C2 to C3. Two-year occlusion rates were 93.7, 90.9, and 91.5% for NBCA, RFA, and EVLA, respectively. NBCA-treated patients experienced the least complications, with bruising, phlebitis, and pain being the most prevalent. Quality of life improved equally in all three modalities. The authors concluded that NBCA is simple to administer, safe, and effective even without compression stockings. The review was limited by lack of randomization for most included studies, and inclusion of products not currently FDA-approved. Further studies are required to assess longer-term benefit and the effect of anticoagulation on vein obliteration.

Eroglu and Yasim (2018) conducted an RCT to compare early and two-year results for NBCA using the VariClose Vein Sealing System (Biolas, FG Grup, Turkey), RFA, and EVLA in the

treatment of varicose veins. The primary endpoint was the occlusion rate, and secondary endpoints were incidence of complications, and patient satisfaction, including freedom from pain during and after the procedure, complications observed, time to return-to-work and change in VCSS scores. A total of 525 patients were randomized (175 patients in each treatment arm) and 456 patients (NBCA, n=168; RFA, n=149; and EVLA, n=139) had evaluable results i.e., post-procedural ultrasounds and assessments completed at 2 days, and 6, 12 and 24 months. Occlusion rates were similar at 6, 12, and 24 months (6 months [NBCA 98.1%, RFA 94.1%, and EVLA 95.1%, p=0.14], 1 year [NBCA 94.7%, RFA 92.5%, and EVLA 94.2%, p=0.72], 2 years [NBCA 92.6%, RFA 90.9%, and EVLA 91.5%, p=0.89]). Peri-procedural pain was significantly lower after NBCA (p<0.001) but complication rates (DVT, bleeding, and phlebitis) were similar. Time to return-to-work was shortest after NBCA (NBCA 1.04 days, RFA 1.56 days and EVLA 1.31 days (p<0.001) with 95% (NBCA), 50% (RFA) and 75% (EVLA) of patients returning to work on Day 1. Pre-procedural VCSSs were the same in all groups. A decrease was observed in VCSS values in all groups at 6 months, and this persisted at 1 and 2 years. However, VCSS scores at 6 months and 2 years were significantly lower in the NBCA group (p<0.001). Foam sclerotherapy was subsequently applied to varicose tributaries in 18 patients from all groups. The authors concluded that no differences were observed in occlusion rates between the three modalities, but NBCA appeared superior with respect to peri-procedural pain, return-to-work and decreased VCSS. Limitations of this study include that the individuals who performed the procedures were also those who completed the evaluations, the number of patients lost to follow-up varied between the treatment arms, and the short follow-up period. Additional multi-center randomized trials with longer follow-up are needed to further evaluate NBCA in the treatment of varicose veins. Currently, the VariClose Vein Sealing System (Biolas, FG Grup, Turkey) is under research in countries other than the United States and has neither been approved nor cleared for marketing by the FDA.

~~Morrison et al. (2018) reported 36-month outcomes of the VeClose randomized controlled trial, a multicenter, prospective, randomized controlled trial in which 222 symptomatic patients with incompetent great saphenous veins were assigned to either cyanoacrylate closure or radiofrequency ablation. The primary endpoint, complete closure of the target great saphenous vein, was determined using duplex ultrasound examination starting from three-month visit. At month 36, the great saphenous vein closure rates were 94.4% for the cyanoacrylate closure group and 91.9% for the radiofrequency ablation group. Stable improvement in symptoms and quality of life was observed in both groups. Adverse event rates between the 24- and 36-month visits were similar between the groups as were serious adverse events which were infrequent and judged unrelated to either the device or the procedure in both groups. In the authors' opinion, the results of this trial continue to demonstrate the safety and efficacy of cyanoacrylate closure for the treatment of great saphenous vein incompetence with great saphenous vein closure rate at 36 months similar to that of radiofrequency ablation. Follow-up of the patient cohorts post-procedure will continue up to 60 months. This study was also included in the Hayes report (2019).~~

~~Gibson et al. (2018a) reported 24-month results from the randomized trial of cyanoacrylate closure (CAC) versus radiofrequency ablation (RFA) for the treatment of incompetent GSVs (VeClose trial). Of 222 randomized patients, 171 completed the 24-month follow-up, which included 87 from the CAC group and 84 from the RFA group. The 24-month complete closure rate was 95.3% in the CAC group and 94.0% in the RFA group, demonstrating continued noninferiority of CAC compared with RFA (P = .0034). Symptoms and quality of life improved similarly in both groups. No clinically significant device- or procedure-related late adverse events were reported. The authors concluded that both CAC and RFA were effective in closure of the target GSV, resulting in similar and significant improvements in the patient's quality of life through 24 months, suggesting that CAC of~~

~~the GSV is safe and durable out to 2 years. Longer-term outcomes from randomized controlled trials are needed. This study was also included in the Hayes report (2019).~~

Gibson et al. (2018b) reported three-month ~~data of~~**outcomes from** a post-market ~~evaluation~~ **case series study** of endovenous cyanoacrylate closure ~~of~~ **by** the VenaSeal system (the WAVES study). Fifty subjects with symptomatic GSV, SSV, and/or accessory saphenous vein incompetence were treated with the VenaSeal system with no post procedure compression stockings. Concomitant procedures were not allowed as part of the original study protocol. Treating physicians predicted the type and nature of any concomitant procedures that they would usually perform at the time of ablation, if not limited by the constraints of the study. Evaluations were performed at one week, one and three months and included duplex ultrasound, numeric pain rating scale, revised ~~venous clinical severity score~~**VCSS**, the ~~Aberdeen Varicose Vein Questionnaire~~**AVVQ**, and time to return to work and normal activities. At the three-month visit, the need for and type of adjunctive procedures were recorded. Complete closure at three months was achieved in 70 (99%) of the treated veins (48 ~~great saphenous veins~~**GSVs**, 14 accessory saphenous veins, eight ~~small saphenous veins~~**SSVs**). Revised ~~venous clinical severity score~~**VCSS** improved from 6.4 ± 2.2 to 1.8 ± 1.5 (P < .001) and ~~Aberdeen Varicose Vein Questionnaire~~**AVVQ** from 17.3 ± 7.9 to 6.5 ± 7.2 (P < .0001). Sixty-six percent of patients underwent tributary treatment at three months. The percentage of patients who required adjunctive treatments at three months was lower than had been predicted by the treating physicians (65% versus 96%, p=.0002). The authors reported that closure rates were high in the absence of the use of compression stockings or side branch treatment. Improvement in ~~quality of life~~**QoL** was significant, and the need for and extent of concomitant procedures was significantly less than had been predicted by the treating physicians. Additional studies with larger patient populations are needed to further evaluate the need for concomitant procedures with the VenaSeal system. **These findings are limited by lack of comparison group undergoing a different treatment.** This study was also included in the Hayes report (20~~19~~**20; updated 2021**).

Gibson and Ferris (2017b) reported results of ~~the~~a prospective case series study (the WAVES study) of cyanoacrylate closure for the treatment of ~~great saphenous veins~~GSVs, ~~small saphenous veins~~SSVs, 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~~GSV, 14 accessory saphenous veins, and 8 ~~small saphenous veins~~SSVs) had complete closure by duplex ultrasound at seven days and one month. Mean time to return to work and normal activities was 0.2 ± 1.1 and 2.4 ± 4.1 days, respectively. The revised ~~venous clinical severity score~~VCSS was improved to 1.8 ± 1.4 (p < .001) and ~~Aberdeen Varicose Vein Questionnaire~~AVVQ score to 8.9 ± 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~~RCTs with a larger patient population and longer follow-up periods are needed to validate findings. The findings of this study are limited by lack of comparison group undergoing a different treatment approach. This study was also included in the Hayes report (20~~19~~20; updated 2021).

~~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. This study was also included in the Hayes report (2019).~~

~~The VeClose study (Morrison et al., 2015) was a prospective, multicenter randomized controlled U.S. pivotal trial which compared cyanoacrylate adhesive (VenaSeal®, Medtronic) to radiofrequency thermal ablation (ClosureFast®, 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. This study was also included in the Hayes report (2019).~~

~~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 ± 1.1 and 2.4 ± 4.1 days, respectively. The revised venous clinical severity score was improved to 1.8 ± 1.4 (p < .001) and Aberdeen Varicose Vein Questionnaire score to 8.9 ± 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. This study was also included in the Hayes report (2019).~~

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~~**GSV**. One, three, and 12 months closure rates were 87.1, 91.7, and 92.2% for ~~endovenous laser ablation~~**EVLA** 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~~**GSVs**. This study was also included in the Hayes report (2019**; updated 2021**).

Almeida et al. (2015) evaluated the safety and effectiveness of endovenous cyanoacrylate-based embolization of incompetent ~~great saphenous veins~~**GSVs in a case series study of** ~~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~~**GSV** 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~~**VCSS** improved in all patients from a mean of 6.1 ± 2.7 at baseline to 1.3 ± 1.1, 1.5 ± 1.4 and 2.7 ± 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 **and lack of comparison groups are** ~~is a~~ limitation**s** to this study. This study was also included in the Hayes report (2019**; updated 2021**).

A prospective multicenter **case series** study was conducted on 78 patients with GSV reflux using cyanoacrylate embolization (Proebstle et al., 2015). Clinical examination, ~~quality of life~~**QoL** 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 ~~Â±~~ 2.3 at baseline to 1.1 ~~Â±~~ 1.3 at 12 months. ~~Aberdeen Varicose Vein Questionnaire~~**AVVQ** score showed an improvement from 16.3 at baseline to 6.7 at 12 months (P < .0001). Side effects were generally mild; a phlebitic reaction occurred in eight cases (11.4%) with a median duration of 6.5 days (range, 2-12 days). Pain without a phlebitic 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. This study was also included in the Hayes report (20**20**~~19~~**; updated 2021**).

~~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

Evidence in peer review literature evaluating endovenous foam sclerotherapy for the treatment of truncal superficial veins in the lower extremities is limited and does not support a benefit compared to established therapies. Future robust RCTs are warranted along with long-term outcomes to establish the safety and efficacy of this procedure.

In an updated Cochrane review, Whing et al. (2021) compared interventions for treating varicosities of the GSV. The review included 24 RCTs with 5135 participants who underwent EVLA, RFA, EVSA, UGFS, cyanoacrylate glue, MOCA, or high ligation and stripping. The review compared EVLA and UGFS and found technical success may be better in EVLA patients up to 5 years and over five years. Recurrence rates had no clear difference up to 3 years and at five years. The authors state there were a relatively small number of studies for comparison and differences in outcome definitions and time points reported limited their conclusions. Future studies which provide more evidence on the breadth of treatments are recommended by the authors. Lawaetz et al. (2017) and Vähäaho et al. (2018), which were previously cited in this policy, are included in this review.

In an ECRI Clinical Evidence Assessment (2020), Varithena injectable foam was found to improve symptoms and appearance of varicose veins when compared to placebo or other unspecified sclerotherapy agents. Evidence was based on three double-blind and one open-label, multicenter, RCTs. A small open-label extension of one of the RCTs found Varithena's beneficial effects were sustained at 1-year follow-up. A separate cohort study found patients had better vein occlusion rates with high ligation surgery than with Varithena at 1-year follow-up. Adverse effects included pain, thrombophlebitis, bruising and thrombus in nontarget vessels and were considered minor. The report notes that longer-term, independent RCTs would be useful to confirm results and to compare Varithena with other varicose vein treatments because no data were available on RFA or laser therapy.

A Hayes Health Technology Assessment (2019) researched 6 clinical studies (n=77-399) that evaluated the efficacy or safety of polidocanol endovenous microfoam (PEM) 1% in treating varicose veins. Eligible studies included five RCTs and one case series. The patients included in the studies had SFJ, GSV or SSV incompetence. The assessment concluded there was a low-quality body of evidence that suggested PEM 1% may provide relief of symptoms and result in occlusion and elimination of reflux. The authors concluded that this approach has potential but unproven benefit. Additionally, substantial uncertainty remains regarding the effectiveness of PEM 1% in relation to other sclerosants and other surgical approaches. The report recommended more well-designed, independent RCTs to further establish the comparative safety and effectiveness of PEM 1%, identify optimal patient selection, and determine the durability of its beneficial effects. (Hayes, 2019; updated 2021).

~~In a 5-year follow-up of a randomized clinical trial comparing open surgery, ultrasound guided foam sclerotherapy (UGFS) and endovenous laser ablation (EVLA) for great saphenous varicose veins, Vähäaho et al. (2018) evaluated long-term results of surgery, EVLA and~~

~~UGFS in the treatment of GSV reflux. Patients with symptomatic GSV reflux were randomized to undergo either open surgery, EVLA or UGFS. The main outcome measure was the occlusion rate of the GSV at 5 years after operation. The study included 196 patients; of these, 166 (84·7 per cent) participated in the 5-year follow-up. At 5 years, the GSV occlusion rate was 96 (95 per cent c.i. 91 to 100) per cent in the open surgery group, 89 (82 to 98) per cent after EVLA and 51 (38 to 64) per cent after UGFS (P < 0·001). For patients who had received no additional treatment during follow-up, the occlusion rates were 96 per cent (46 of 48), 89 per cent (51 of 57) and 41 per cent (16 of 39) respectively. UGFS without further GSV treatment was successful in only 16 of 59 patients (27 percent) at 5 years. The authors concluded that UGFS has significantly inferior occlusion rates compared with open surgery or EVLA, and results in additional treatments.~~

~~Lawaetz et al. (2017) compared the outcomes 5 years after treatment of varicose veins with endovenous radiofrequency ablation (RFA), endovenous laser ablation (EVLA), ultrasound guided foam sclerotherapy (UGFS) or high ligation and stripping (HL/S) by assessing technical efficacy, clinical recurrence and the rate of reoperations. Five hundred patients (580 legs) with GSV reflux and varicose veins were randomized to one of the 4 treatments. Follow-up included clinical and duplex ultrasound examinations. During 5 years there was a difference in the rate of GSV recanalization, recurrence and reoperations across the groups, Kaplan Meier (KM) P<0.001, P<0.01, P<0.001 respectively. Thus 8 in the RFA group (Kaplan Meier [KM] estimate 5.8%), 8 in the EVLA group (KM estimate 6.8%), 37 (KM estimate 31.5%) in the UGFS group and 8 in the HL/S group (KM estimate 6.3%) of GSVs recanalized or had a failed stripping procedure. Nineteen (RFA) (KM estimate 18.7%), 42 (EVLA) (KM estimate 38.6%), 28 (UGFS) (KM estimate 31.7%) and 38 (HL/S) (KM estimate 34.6%) legs developed recurrent varicose veins. Within 5 years after treatment, 19 (RFA) (KM estimate 17%), 19 (EVLA) (KM estimate 18.7%), 43 (UGFS) (KM estimate 37.7%) and 25 (HL/S) (KM estimate 23.4%) legs were retreated. More recanalizations of the GSV occurred after UGFS and no difference in the technical efficacy was found between the other modalities during 5-year follow-up. According to the authors, the higher frequency of clinical recurrence after EVLA and HL/S cannot be explained and requires confirmation in other studies.~~

Gibson et al. (2017**a**) conducted a randomized, placebo-controlled, multicenter study to evaluate the safety and efficacy of ~~polidocanol endovenous microfoam~~**PEM** (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, achiness, 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 ≤ 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~~**RCTs** with longer-term outcomes and comparisons to established treatments for varicose veins are needed to evaluate the clinical utility of this procedure. **The findings of this study are limited by the short follow up and lack of comparison with an established therapy.**

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. Furthermore, this study did not compare endovenous microfoam to established treatment for varicose veins.

In a multicenter, randomized, placebo-controlled, blinded study in patients with ~~great saphenous vein~~**GSV** 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%~~)~~**, or** ~~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~~ **PEM** 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~~**SFJ** 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.~~ While these results appear promising, PEM outcomes were compared with placebo and with a short follow-up period. Additional ~~randomized controlled trials~~**RCTs** comparing PEM outcomes with other established varicose vein treatment outcomes, and with a longer follow-up period are needed.

King et al. (2015) ~~designed~~ **reported** a multicenter, parallel group study (VANISH-1), to determine if a single administration of ≤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 studies with comparisons to other varicose vein treatments and over a longer period of time are needed before determining the safety and efficacy of this procedure.

In the VANISH-2 trial, Todd et al. (2014) evaluated the efficacy and safety of ~~polidocanol endovenous microfoam~~**PEM** in treatment of symptoms and appearance in patients with ~~saphenofemoral junction~~**SFJ** incompetence due to reflux of the ~~great saphenous vein~~**GSV** or major accessory veins. Patients were randomized equally to receive ~~polidocanol endovenous microfoam~~**PEM** 0.5%, ~~polidocanol endovenous microfoam~~**PEM** 1.0% or placebo. In 232 treated patients, ~~polidocanol endovenous microfoam~~**PEM** 0.5% and ~~polidocanol endovenous microfoam~~**PEM** 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~~**PEM**-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~~**PEM** provided clinically meaningful benefit in treating symptoms and appearance in patients with varicose veins. However, longer-term outcomes with comparisons between PEM and other established treatments for varicose veins 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. Furthermore, this study did not compare endovenous microfoam to established treatment for varicose veins.~~

~~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.~~

Clinical Practice Guidelines

~~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., 2017c) 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~~**EVTA** (laser or radiofrequency) or ~~ultrasound-guided foam sclerotherapy~~**UGFS** to eliminate symptomatology (Recommendation Grade 1C).

The American College of Phlebology Guidelines Committee (**2016) updated their** ~~2014) created a white paper to summarize the~~ evidence-based recommendations ~~in the Gloviczki et al. guidelines (2011) as well as many other current studies~~ **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~~**EVTA** (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).

European Society for Vascular Surgery (ESVS)

The ESVS released a clinical practice guideline for management of chronic venous disease (Wittens et al., 2015). The guidelines do not recommend liquid or foam sclerotherapy as the first-choice treatment for chronic venous disease C2-C6 due to saphenous vein incompetence. Per the guideline, this procedure should only be used as primary treatment in selected cases, such as those not eligible for surgery or endovenous ablation, and elderly, frail patients with venous ulcers. Cyanoacrylate glue injection and MOCA are not addressed due to lack of publications. The guidelines note that USGF has been used successfully in the treatment of recurrence, although with lower success rates compared with laser ablation.

National Institute for Health and Care Excellence (NICE)

In 2020, the National Institute for Health and Care Excellence (NICE) released an update to their guidance on Cyanoacrylate Glue Occlusion for Varicose Veins. The updated guidance states that current evidence on the safety and efficacy of cyanoacrylate glue occlusion for varicose veins is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. In addition, the guideline states physicians should: 1) only perform the procedure after appropriate training and experience in the use of venous ultrasound; 2) discuss the available options with the patient before making a decision; and 3) follow their hospital's policies regarding performing procedures and monitoring results.

In an updated guideline on endovenous MOCA for varicose veins, NICE (2016) states that current evidence on the safety and efficacy of endovenous MOCA 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.

The NICE 2013 interventional procedure guidance on UGFS 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 GSVs or ligation with or without stripping of the SSVs, and phlebectomy). The NICE 2013 clinical guideline on the diagnosis and treatment of varicose veins adds that if endovenous ablation is unsuitable, offer UGFS.

Society for Vascular Surgery (SVS)/American Venous Forum (AVF) /American Vein and Lymphatic Society (AVLS)/ Society of Interventional Radiology (SIR)

The SVS, AVF, AVLS, and SIR developed the appropriate use criteria (AUC) for chronic lower extremity venous disease using the RAND/UCLA Appropriateness Method incorporating best available evidence with expert opinion and engaging a panel of experts in the field through a modified Delphi exercise (Masuda et al. 2020). The consensus does not appear to be based on a systematic review of the literature. One hundred and nineteen scenarios were rated on a scale of one to nine by an expert panel, with one being never appropriate and nine being appropriate. The panelists rated ablation for axial reflux of the GSV, with or without SFJ reflux, in symptomatic patients, CEAP classes 2-6 as appropriate. Per the AUC, when accompanied by no SFJ reflux (the junction is either assumed or proven to be competent or previously interrupted and communicates with the GSV through incompetent thigh perforators or other sources of collateral flow) the remaining refluxing GSV may be the source of recurrent symptoms. Therefore, for axial GSV reflux, ablating the GSV will likely lead to decreased recurrence even if the SFJ shows no reflux. The authors note that the AUC statements were intended to serve as a guide to patient care, particularly in areas where high quality evidence is lacking and was not meant to be a guide that addresses all clinical situations.

The SVS and AVF released joint clinical practice guidelines regarding the care of patients with venous leg ulcers (O'Donnell et al., 2014). For patients with a venous leg ulcer (C6), and incompetent superficial veins that have reflux to the ulcer bed in addition to pathological perforating veins (>500ms reflux duration and diameter of >3.5mm), that are located beneath or associated with the ulcer bed, the guideline recommends ablation of both the incompetent superficial veins and perforator veins in addition to standard compressive therapy to aid in ulcer healing and prevent recurrence. For patients who are at risk for a venous leg ulcer (C4b), or have a healed venous ulcer (C5), and have axial reflux directed to the bed of the affected skin/ulcer, the guidelines recommend ablation of the incompetent superficial veins in addition to standard compressive therapy.

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~~EVTA 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~~EVTA over chemical ablation with foam. The guidelines do not discuss MOCA. The ~~policy~~guideline also states that patients who undergo high ligation alone of the ~~great saphenous vein (~~GSV~~)~~ have

recurrent reflux in the residual GSV. ~~This~~ **which may** causes~~ new symptoms and increases the risk of reoperation.**

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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. (Accessed **April 13, 2022**~~January 21, 2020~~)

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 **April 13, 2022**~~January 21, 2020~~)

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/label/2013/205098s000lbl.pdf

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Policy History/Revision Information

Date	Summary of Changes

TBD	**Coverage Rationale**
	Varicose Vein Ablative and Stripping Procedures
	• Revised coverage criteria; replaced criterion requiring
	  ○ "The individual must have documented venous stasis dermatitis" with "the individual must have documented venous stasis dermatitis *causing Functional or Physical Impairment*"
	  ○ "The Small Saphenous Vein (SSV) or Accessory Veins must measure 5 mm or greater in diameter immediately below the *sapheno-popliteal* junction" with "the Small Saphenous Vein (SSV) or Accessory Veins must measure 5 mm or greater in diameter immediately below the *appropriate* junction"
	Ligation Procedures
	• Added language to indicate ligation, subfascial, endoscopic surgery for treatment of perforating veins associated with chronic Venous Insufficiency is proven and medically necessary in certain circumstances; for medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Ligation, Subfascial, Endoscopic, Perforating Vein
	Ambulatory Phlebectomy
	• Added language to indicate ambulatory phlebectomy for treating varicose veins is proven and medically necessary in certain circumstances; for medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Ambulatory Phlebectomy, Varicose Vein for:
	  ○ Hook Phlebectomy
	  ○ Microphlebectomy
	  ○ Mini Phlebectomy
	  ○ Stab Avulsion
	  ○ Stab Phlebectomy
	Definitions
	• Added definition of "Sclerotherapy"
	Applicable Codes
	• Added CPT codes 36468, 36470, 36471, 37500, 37735, 37760, 37761, 37765, 37766, and 37785
	• Added language to indicate:
	  ○ Adherence to AMA coding guidance is required when requesting endovenous ablation procedures:
	  ▪ Per AMA coding guidance, the initial incompetent vein treated (e.g., 36475) may only be requested once per extremity; for endovenous ablation, treatment of subsequent incompetent veins in the same extremity as the initial vein treated (e.g., 36476), only one add-on code per extremity may be requested, regardless of the number of additional vein(s) treated
	  ▪ Therefore, only one primary code may be requested for the initial vein treated, and only one add-on code per extremity may be requested for any subsequent vein(s) treated
	  ○ CPT code 36468 for sclerosant treatment for spider veins is considered cosmetic (does not improve a functional, physical or physiological impairment)

Date	Summary of Changes
	○ CPT codes 36470 and 36471 are covered for sclerotherapy up to 3 sessions per leg within a year: ▪ More than 3 sessions per leg within a year is considered cosmetic (does not improve a functional, physical or physiological impairment); cosmetic sclerotherapy is excluded ▪ A session is defined as one date of service in which sclerotherapy (CPT codes 36470 and 36471) is performed ▪ A year is defined as a rolling 12 months (365 days) **Benefit Considerations** ***Coverage Limitations and Exclusions*** • Added language for Sclerotherapy Treatment of Veins to indicate: ○ Cosmetic sclerotherapy is excluded ○ Sclerotherapy up to 3 sessions per leg within a year is covered; more than 3 sessions per leg within a year is considered cosmetic ○ A session is defined as one date of service in which sclerotherapy (CPT codes 36470 and 36471) is performed ○ A year is defined as a rolling 12 months (365 days) **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS117LA.O

Instructions for Use

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