UnitedHealthcare Oxford

UnitedHealthcare® Oxford
Clinical Policy

Surgical and Ablative Procedures for Venous Insufficiency and Varicose Veins

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➲ Instructions for Use

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Coverage Rationale

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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
  - 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 5.5mm or greater when measured at the proximal thigh immediately below the sapheno-femoral junction via Duplex Ultrasonography (Navarro et al. 2002)
  - The SSV or Accessory Veins must measure 5 mm or greater in diameter immediately below the appropriate junction
- Duration of reflux, in the standing or reverse Trendelenburg position that meets the following parameters:
  - Greater than or equal to 500 milliseconds (ms) for the GSV, SSV or principal tributaries
  - Some Duplex Ultrasound readings will describe this as moderate to severe reflux which will be acceptable

Refer to the 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 3.5mm or greater; and
- Perforating veins > 350 ms; and
- Perforating vein lies beneath a healed or active venous stasis ulcer

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
- Endovenous mechanochemical ablation (MOCA) of Varicose Veins
- Porcine bioprosthetic valve (e.g., VenoValve) implantation into the femoral vein for treatment of deep vein reflux associated with chronic venous insufficiency

Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

CPT Codes*	Required Clinical Information
Surgical and Ablative Procedures for Venous Insufficiency and Varicose Veins	

36470
36471
36473
36474
36475
36476
36478
36479
37700
37718
37722
37780
	Medical notes documenting the following, when applicable:
	• Diagnosis
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms; including onset, duration, frequency, and which extremity (right, left, or both)
	• Pain or other symptoms that interfere with activities of daily living (ADL) related to vein disease, including duration
	• Functional disability(ies), as documented on a validated functional disability scale, interfering with the ability to stand or sit for long periods of time
	• Relevant medical history, including:
	  ○ DVT (deep vein thrombosis)
	  ○ Aneurysm
	  ○ Tortuosity
	• Physical exam, including:
	  ○ Which extremity (right, left, or both)
	  ○ Vein(s) that will be treated [e.g., Great Saphenous Vein (GSV) and Small Saphenous Vein (SSV), etc.]
	  ○ Vein diameter including the specific anatomic location where the measurement was taken (e.g., proximal thigh, proximal calf, etc.)
	  ○ Duration of reflux including the position of member at the time of measurement and the anatomic location where the measurement was taken [e.g., standing, saphenofemoral junction (SFJ)]
	• Reports of recent imaging studies and applicable diagnostic tests
	• Prior non-invasive treatments of the veins that have been tried, failed, or were contraindicated; include the dates, duration, and reason for discontinuation
	• History of prior treatment complications (e.g., recurrent bleeding or significant hemorrhage) including the dates of occurrence
	• History of previous relevant vein procedure(s), if applicable
	• Proposed treatment plan with procedure code, including specific vein(s) that will be treated [e.g., Great Saphenous Vein (GSV) and Small Saphenous Vein (SSV), etc.], which extremity (left, right, or both), and date of procedure for each vein to be treated

*For code descriptions, refer to the Applicable Codes section.

Definitions

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

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

Congenital Anomaly: A physical developmental defect that is present at the time of birth, and that is identified within the first twelve months of birth.

Cosmetic Procedures: Cosmetic Procedure are excluded from coverage. Procedures or services that change or improve appearance without significantly improving physiological function, as determined by us.

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 Procedures when the primary purpose of the procedure is either of the following:
- Treatment of a medical condition.
- Improvement or restoration of physiologic function.

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

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

Reticular Vein: Reticular Veins are dilated dermal veins less than 4 mm 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 pregnancy. The term Sickness includes mental illness or substance-related and addictive disorders, regardless of the cause or origin of the mental illness or substance-related and addictive disorder.

Small Saphenous Vein: Superficial vein of the calf.

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

Stripping: Surgical removal of superficial veins.

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

Telangiectasia: *See Spider Vein.*

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

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

- Deep veins: 1 sec.
- Superficial veins: 0.5 sec.
- Perforator veins: 0.35 sec.

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

Applicable Codes

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

Coding Clarifications:

- 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 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).

CPT Code	Description
0744T	Insertion of bioprosthetic valve, open, femoral vein, including duplex ultrasound imaging guidance, when performed, including autogenous or nonautogenous patch graft (e.g., polyester, ePTFE, bovine pericardium), when performed

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
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 sapheno-femoral 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
37765	Stab phlebectomy of varicose veins, 1 extremity; 10-20 stab incisions
37766	Stab phlebectomy of varicose veins, 1 extremity; more than 20 incisions
37780	Ligation and division of short saphenous vein at sapheno-popliteal junction
37785	Ligation, division, and/or excision of varicose vein cluster(s), 1 leg
37799	Unlisted procedure, vascular surgery

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Description of Services

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

Duplex ultrasound is considered the gold standard for diagnosis of superficial venous incompetence. The CEAP (clinical, etiology, anatomy, pathophysiology) 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], 2020)

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), (2020))

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, 2022) 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 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.
- Treatment for Spider Veins and/or Telangiectasias is considered to be cosmetic and therefore excluded from coverage.
- Endovenous Ablation (radiofrequency and/or laser) of either reticular or telangiectatic veins is not reconstructive and unproven not medically necessary and therefore 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 EVLA or radiofrequency ablation, and 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) 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 this meta-analysis.

Boersma et al. (2016) performed a systematic review and meta-analysis of treatment modalities for small saphenous vein insufficiency. The review included 49 studies (5 RCTs, 44 cohort studies) reporting on the different treatment modalities: surgery (n = 9), EVLA (n = 28), RFA (n = 9), 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 SSV. 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 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 recanalizations and five recurrences of the GSV. 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 and lack of comparison group.

In a systematic review and meta-analysis of RCT of endovenous ablation (EVA) of the 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 RFA, and five employed 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 EVLA for the treatment of venous insufficiency of the GSV, 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 six 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 GSV, reducing postoperative pain and hospital stay.

Woźniak et al. (2016) conducted a cohort study of complications and failure of EVLA and RFA in a 5-year follow-up. One hundred ten adult participants with varicose veins clinical grade C2 to C6, treated for isolated GSV or 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.

Chaar et al. (2011) conducted a retrospective cohort analysis of patients undergoing endovenous laser therapy on the GSV, 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 three 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 two GSVs (group GR) partially recanalized by three months (GSV ablated in 49/51 (96%) limbs versus 50/51 (98%) limbs in GP [$p = 0.2$]). Improvements in AVVSS at three 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 one- 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 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, 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 chronic venous disease (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 GSV. Similarly, a 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 five 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 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 six 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 RCT to assess whether more extensive GSV ablation enhances resolution and influences symptom improvement in patients with previous above-knee (AK) 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 (six 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 EVLT. There were no significant differences in preoperative characteristics between the groups treated with RFA or EVLT. Patients were reexamined within three 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 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. Postablation, 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 preablation) 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 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 SFJ reflux in patients with CVD and a normal 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 one 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 one, a main tributary in one and four 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 one 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 SF 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). Neovascularization (serpentine tributaries arising from the ligated 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 seven 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 SFJ on duplex imaging at two 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.

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; GSV, at the SFJ, thigh, upper calf, and lower calf; and lesser saphenous vein, at the 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 four patients, 5 GSV (4.8%) were recanalized completely after one week, after three months (n = 3), or after 12 months. Another five GSV (4.8%) in five patients exhibited incomplete proximal recanalization over the 12 months of follow-up. Finally, nine 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 SFJ and truncal GSV incompetence. Eighty-five consecutive patients aged 28 to 82 (mean, 46.2) years; 112 lower limbs with 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 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 SFJ and reduce the incidence of PE. The two types of surgical treatment were ligation of the GSV at the 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 six weeks and six 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 DVT and PE development as compared to surgical treatment with ligation of the GSV at the SFJ or ligation and stripping.

Chandler et al. (2000) conducted a prospective, comparative study to evaluate the effect of extended SFJ ligation when the 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 six 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 six 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 one 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 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 DVT, 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.

A Hayes Health Technology Assessment states MOCA with the ClariVein infusion catheter appears safe and effective over the short-term but the low-quality body of evidence does not allow conclusions to be drawn regarding the long-term durability of the procedure. The report states that MOCA resulted in slightly poorer technical outcomes and higher rates of recanalization than thermal ablation and surgical procedures. The report recommends future well-designed trials with larger sample sizes that compare MOCA using the ClariVein infusion catheter with clinical alternatives with a long-term follow-up. (Hayes, 2022)

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 one 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 six (5-8) to zero (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 five 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 MOCA, 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.

Kim et al. (2017) evaluated in a case series whether early efficacy in endovenous MOCA is maintained at 24 months. Patients with reflux in the 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 CEAP class and 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 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 VCSS (p < .001) for all time intervals. Early high occlusion rate with MOCA is associated with significant clinical improvement, which was maintained at 24 months. According to the authors, this finding is suggestive of a good option for the treatment of 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 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 SSV incompetence, and recurrent GSV incompetence. Primary outcome was anatomic success. Secondary outcomes were initial technical success, VCSS, AVVQ score, and complications. Fifteen articles met the inclusion criteria. Pooled anatomic success for MOCA and CAVA was 94.7% and 94.8% at six months and 94.1% and 89.0% at one year, respectively. VCSS and 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 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 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 GSV and 254 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 six 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 two and three 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 RCTs are available studying the anatomical success after MOCA compared to the endothermal ablation.

Witte et al. (2017b) reported midterm results of MOCA for treating 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 (four weeks and one, two, and three years) using duplex ultrasound, the CEAP classification, the VCSS, the RAND Short Form 36-Item Health Survey (RAND-SF36), and the AVVQ. Primary outcome measures were clinical and anatomic success. Secondary outcome measures included general and disease-specific 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 one, two, and three years, respectively. The VCSS improved at all time intervals compared to the preprocedure median. The clinical success at three 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 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.

Vun et al. (2015) assessed the efficacy of the ClariVein system for the treatment of superficial vein incompetence. Fifty-one GSV and six SSV 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 short-term follow-up. Further data on long-term clinical outcomes is needed.

In a prospective case series, Boersma et al. (2013) evaluated the feasibility, safety and 1-year results of MOCA of 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 control group, small sample size and short-term follow-up.

In a prospective comparison study, van Eekeren et al. (2013) evaluated postoperative pain and QoL after RFA and MOCA for 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 six weeks, patients in both groups perceived an improved change in health status and an improved disease-specific QoL. This study is limited by lack of randomization, small sample size and short-term follow-up.

In a pilot study, van Eekeren et al. (2011) evaluated the feasibility and safety of endovenous MOCA for the treatment of 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 VCSS were assessed 6 weeks after the treatment. Initial technical success of MOCA was 100%. There were no major adverse events. Duplex ultrasonography at six 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 six 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.

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)

A 2022 Hayes Health Technology Assessment evaluated nine clinical studies on the efficacy and safety of cyanoacrylate embolization with the VenaSeal Closure System. The evidence included three RCTs and six retrospective comparative studies. The conclusion states that a low-quality body of evidence suggests VenaSeal has a high level of successful venous closure for at least one year that may result in reduced symptom severity and improved QoL. Efficacy and safety may be comparable to RFA, EVLA, and MOCA; however, substantial uncertainly remains regarding its effectiveness due to the lack of well-designed comparative studies and limited follow-up beyond one year. The authors overall conclusion is that cyanoacrylate embolization with the VenaSeal Closure System has potential but unproven benefits.

Amshar et al. (2022) conducted a systematic review and meta-analysis to evaluate the efficacy, intervention time, and safety of cyanoacrylate embolization (CAE) in comparison to EVLA in treatment of saphenous vein insufficiency. Efficacy was determined by venous closure rate one-year post-intervention and VCSS one-year post-intervention. Safety was determined by rates of periprocedural pain, skin pigmentation, nerve damage, phlebitis, DVT and ecchymosis. Two randomized-controlled trials and three cohort studies were included in this review. The total number of individuals was 1,432 (710 CAE and 722 EVLA). Venous closure rates and VCSS did not differ significantly between CAE group and EVLA group. Pooled data showed that CAE group was associated with less periprocedural pain score ($p < 0.001$), lower skin pigmentation rates (0.60% vs. 4.46%; $p = 0.008$), and lower nerve damage rates (0% vs. 3.94%; $p = 0.007$). Rates of phlebitis, DVT, and ecchymosis did not differ significantly between the two groups. In addition, intervention time was significantly faster in CAE group compared to EVLA group ($p < 0.001$). The authors concluded CAE was not inferior to EVLA in terms of efficacy and CAE showed less adverse effects occurrence rates of periprocedural pain, skin pigmentation, and nerve damage complications. Additionally, intervention time is stated to be faster with CAE compared to EVLA. The authors note that future RCTS with larger sample sizes and longer post-procedural follow-up time are needed. Additionally, efficacy outcomes were limited to one year and longer-term outcome data would provide additional evidence of efficacy. Bozkurt and Yilmaz (2016), and Eroglu and Yasim (2018) which were previously cited in this policy, are included in this review. 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.

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.

Joh et al. (2021) conducted an open-label multicenter, prospective, RCT 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 one, three, six, and 12 months postoperatively using duplex ultrasound. The primary endpoint of the study was to evaluate complete closure of the target vein at three months. Ecchymosis grades, VCSS, AVVQ scores 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 (nine 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 three 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 three, 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 three, adverse events, and details of adjunctive procedures. Patient follow-up visits were on day three and at months one, three, six, 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., three 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 three 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 (2022). The individual studies are listed below:

- Morrison et al. (2015) reported three-month outcomes from the VeClose trial. No adjunctive procedures such as phlebectomy and UGFS were allowed until after the month three 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 three 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 nine 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 EVLA)with mean procedure times of 25.7, 23.2, and 28.7 minutes, respectively. Mean recruitment period was nine 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.

Gibson et al. (2018b) reported three-month outcomes from a post-market case series study of endovenous cyanoacrylate closure 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 VCSS, the 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 GSVs, 14 accessory saphenous veins, eight SSV). Revised VCSS improved from 6.4 ±2.2 to 1.8 ±1.5 ($p < .001$) and 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 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. (2022)

Gibson and Ferris (2017) reported results of a prospective case series study (the WAVES study) of cyanoacrylate closure for the treatment of GSVs, SSVs, and/or accessory saphenous veins up to 20 mm in diameter (n = 50). Compression stockings post-procedure were not utilized. Patients returned at one week and one month for follow-up. All treated veins (48 GSV, 14 accessory saphenous veins, and eight 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 VCSS was improved to 1.8 ±1.4 ($p < .001$) and 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. 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. (2022)

Almeida et al. (2015) evaluated the safety and effectiveness of endovenous cyanoacrylate-based embolization of incompetent GSVs in a case series study of 38 patients. At 12 months, 36 patients were available for follow-up and 24 patients at 24 months. Complete occlusion of the treated GSV was confirmed by duplex ultrasound in all patients except for one complete and two partial recanalizations observed at one, three and six 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. 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 six, 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 six, 12 and 24 months, 84%, 78% and 64% were free from leg pain, respectively. In a follow-up study, Almeida et al. (2017) evaluated the long-term safety and effectiveness of endovenous cyanoacrylate (CA)-based closure of incompetent GSV on the twenty-nine individuals that were available for the 36-month follow-up. Complete occlusion of the treated veins was confirmed by ultrasound in all subjects with the exception of two subjects showing recanalization at month one and month three. Kaplan-Meier analysis revealed an occlusion rate at month 36 of 94.7%. The mean VCSS) improved from 6.1 ±2.7 at baseline to 2.2 ±0.4 at month 36 (p < .0001). Pain, edema, and varicosities (VCSS subdomains) improved in 75.9%, 62.1%, and 41.4% of subjects, respectively, at month 36. Overall adverse events were self- limited and mild or moderate. The authors concluded cyanoacrylate adhesive had no reported serious adverse events, had long-term occlusion rates comparable to other thermal and nonthermal methods, and appears to be safe and effective for saphenous vein closure. Small sample size and lack of comparison groups are limitations to this study.

A prospective multicenter case series study was conducted on 78 patients with GSV reflux using cyanoacrylate embolization. (Proebstle et al., 2015) Clinical examination, QoL assessment and duplex ultrasound were performed at two days, one, three, six, 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) VCSS improved from 4.3 ±2.3 at baseline to 1.1 ±1.3 at 12 months. 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.

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 five years and over five years. Recurrence rates had no clear difference up to three 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 six 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 authors overall conclusion is that PEM has potential but unproven benefits. 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 2022).

Gibson et al. (2017a) conducted a randomized, placebo-controlled, multicenter study to evaluate the safety and efficacy of 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 one, four, eight, 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, $p \leq 0.001$). Adverse events included contusion, incision-site hematoma, and limb discomfort. Venous thrombus adverse events were reported as mild and generally resolved without sequelae. Large 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 PEM1%. 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 GSV incompetence and symptomatic and visible superficial venous disease, Vasquez et al. (2017) evaluated the efficacy and safety of PEM 0.5%, 1.0%, or placebo each administered with endovenous thermal ablation. Co-primary endpoints were physician-assessed, and patient-assessed appearance change from baseline to week eight. A total of 117 patients received treatment (38 placebo, 39 PEM 0.5%, 40 PEM 1%). Physician-rated vein appearance at week eight was significantly better with PEM ($p = 0.001$ vs. placebo); patient-assessed appearance trended similarly. In the authors' opinion, PEM provided improvements in clinically meaningful change in patient-assessed and physician-assessed appearance ($p < 0.05$), need for additional treatment ($p < 0.05$), SFJ reflux elimination, symptoms, and QOL. In PEM recipients, the most frequent adverse event was superficial thrombophlebitis (35.4%). While these results appear promising, PEM outcomes were compared with placebo and with a short follow-up period. Additional RCTs comparing PEM outcomes with other established varicose vein treatment outcomes, and with a longer follow-up period are needed.

King et al. (2015) reported a multicenter, parallel group study (VANISH-1), to determine if a single administration of ≤ 15 mL of pharmaceutical-grade 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 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 PEM in treatment of symptoms and appearance in patients with SFJ incompetence due to reflux of the GSV or major accessory veins. Patients were randomized equally to receive PEM 0.5%, PEM 1.0% or placebo. In 232 treated patients, PEM 0.5% and 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 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 PEM provided clinically meaningful benefit in treating symptoms and appearance in patients with varicose veins. However, longer-term outcomes with comparisons between the PEM and other established treatments for varicose veins are needed to evaluate the clinical utility of this procedure.

VenoValve

Evidence in peer review literature evaluating VenoValve porcine bioprosthetic valve for the treatment of chronic venous insufficiency is limited. Future robust RCTs are warranted along with long-term outcomes to establish the safety and efficacy of this procedure.

A 2022 Hayes Emerging Technology Report states published evidence is limited to publications reporting 6-month and 1-year outcomes for 11 patients. The VenoValve will be the first porcine bioprosthetic valve to reach the market in the U.S., and the first device approved to treat CVI, if eventually FDA-approved. VenoValve is currently under investigation in the Surgical Anti-Reflux Venous Valve Endoprosthesis (SAVVE) trial. (NCT04943172)

Ulloa and Glickman (2021) conducted a single-center, prospective, non-randomized, first-in-human trial using a prosthetic venous valve, VenoValve, for patients with severe chronic venous insufficiency (C4b-C6 disease). Ten patients had the prosthetic valve surgically implanted into the femoral vein. Follow-up examinations were conducted postoperatively at two and 14 days and then every 30 days for six months to evaluate feasibility, initial safety and performance outcomes of the VenoValve. Six patients had required bovine patch angioplasty of the vein. Four adverse events occurred, including one case of hematoma at the incision site that was aspirated, two cases of superficial wound infection in C6 patients treated with antibiotics, and one case of a bleeding complication due to warfarin anticoagulation. One patient's VenoValve had thrombosed at five months due to nontherapeutic anticoagulation. Improvements in all five patients who had reached the 6-month follow-up mark with the VenoValve were demonstrated during the study period by decreases in the VCSS (61% decrease from baseline), visual analog scale for pain scores (57% decrease), and reflux time (40% decrease) and a statistically significant improvement in the VEINES-QOL/Sym questionnaire. The patient with the occluded VenoValve had experienced improvements in all areas except for the reflux time. The authors concluded that VenoValve showed promising results with improvements noted in QOL and clinical outcomes. The authors recommended further follow-up and larger studies in the future.

Clinical Practice Guidelines

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 EVTA (laser or radiofrequency) or UGFS to eliminate symptomatology (Recommendation Grade 1C).

The American College of Phlebology Guidelines Committee (2016) updated their evidence-based recommendations for treatment of superficial venous disease of the lower leg. They recommend that named veins [GSV, SSV, 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).

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. (De Maeseneer et al., 2022) The guidelines state that for patients with GSV and SSV incompetence requiring treatment endovenous thermal ablation is recommended as the first-choice treatment, in preference to high ligation/stripping and USGF. However, USGF may be considered for treating saphenous trunks with a diameter less than 6mm. The guidelines note that in long term follow up of comparative studies, treatment with UGFS has been substantially less effective than EVLA, RFA, and surgery in terms of occlusion or absence rates. Additionally, foam sclerotherapy is the technique of choice for anatomical configurations that make endovenous cannulation or advancing the ablation device challenging, and is suitable for treating tortuous, recurrent varicose veins. Mechanochemical ablation and cyanoacrylate adhesive closure may be considered when a non-thermal technique is preferred for patients with GSV incompetence. For patients with GSV incompetence, high ligation/stripping should be considered, if endovenous thermal ablation options are not available. Endovenous non-thermal non tumescent ablation methods may be considered for treatment of SSV incompetence. Additionally, endovenous thermal ablation and USGF may be considered for anterior accessory saphenous vein requiring treatment.

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, and AVLS collaborated to update the 2011 SFS/AVF clinical practice guideline to provide evidence-based recommendations for treating patients with varicose veins of the lower limbs (Gloviczki et al., 2022). Recommendations of the guideline are summarized as follows (not all-inclusive):

- For patients with CVD of the lower extremities, duplex ultrasound scanning is the diagnostic test of choice for evaluation of venous reflux
- Reflux is defined as a minimum value > 500 ms of reversed flow in the superficial truncal veins and the tibial, deep femoral, and perforating veins
- Axial reflux is defined as uninterrupted retrograde venous flow from the groin to the calf, and junctional reflux is limited to the SFJ or SPJ
- Use of the 2020 upgraded CEAP classification of chronic venous disorders is recommended
- "Pathologic" perforating veins in patients with varicose veins (CEAP clinical class C2) includes those with an outward flow duration of ≥ 500 ms and a diameter of ≥ 3.5 mm on duplex ultrasound
- For patients with symptomatic varicose veins and axial reflux in the GSV and SSV, treatment with endovenous ablation over high ligation and stripping is recommended due to less postprocedure pain and morbidity, and an earlier return to regular activity; if the technology or expertise in endovenous ablation is not available or the venous anatomy precludes endovenous treatment, ligation and stripping is recommended
- For patients with symptomatic varicose veins and axial reflux in the GSV, SSV, who place a high priority on the long-term outcomes of treatment (qol and recurrence), treatment with EVLA, RFA, or high ligation and stripping over physician-compounded UGFS is suggested
- For patients with symptomatic axial reflux, both thermal and nonthermal ablation of the GSV and SSV are recommended depending on the available expertise of the treating physician and the preference of the patient

- In patients with symptomatic reflux in the GSV or SSV and associated varicosities, ablation of the refluxing venous trunk, and concomitant phlebectomy, or UGFS of the varicosities with physician-compounded foam or commercial PEM is recommended
- In patients with symptomatic reflux in the GSV or SSV, ablation of the refluxing venous trunk, and staged or UGFS of the varicosities is recommended only if anatomic or medical reasons are present

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.

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. Refer to the following website for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf7/K071468.pdf. (Accessed June 6, 2023)

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 GSV, through endovascular embolization with coaptation. VenaSeal is intended for use in adults with clinically symptomatic venous reflux as diagnosed by duplex ultrasound (DUS). Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140018. (Accessed June 6, 2023)

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 GSV system above and below the knee. Refer to 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

(Accessed June 6, 2023)

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The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2023T0447KK]

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Policy History/Revision Information

Date	Summary of Changes
04/01/2024	**Documentation Requirements** • Updated list of CPT codes with associated documentation requirements; removed 36468 **Supporting Information** • Archived previous policy version OUTPATIENT 013.48

Instructions for Use

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

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