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

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Instructions for Use

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Related Policies

- Cosmetic and Reconstructive Procedures
- Embolization of the Ovarian and Iliac Veins for Pelvic Congestion Syndrome

Application

This Medical Policy only applies to the state of Indiana.

Coverage Rationale

See Benefit Considerations

Varicose Vein Ablative and Stripping Procedures

The initial and subsequent radiofrequency ablation, endovenous laser ablation, stripping, ligation and excision of the great saphenous vein (GSV) and small saphenous veins (SSV) are considered reconstructive, proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® 2021, Apr. 2021 Release, CP: Procedures, Ligation, Subfascial, Endoscopic, Perforating Vein.

Click here to view the InterQual® criteria.

See the Coding Clarifications. 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.

Endovenous mechanochemical ablation (MOCA) of Varicose Veins is unproven and not medically necessary due to insufficient evidence of efficacy.

Ligation Procedures

The following procedure is proven and medically necessary:

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

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

- Ligation, subfascial, endoscopic surgery for treatment of perforating veins associated with chronic Venous Insufficiency. For medical necessity clinical coverage criteria, refer to the InterQual® 2021, Apr. 2021 Release, 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® 2021, Apr. 2021 Release, CP: Procedures, Ambulatory Phlebectomy, Varicose Vein:

- 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

Applicable Codes

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

Coding 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	Description
36465	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; single incompetent extremity truncal vein (e.g., great saphenous vein, accessory saphenous vein)
36466	Injection of non-compounded foam sclerosant with ultrasound compression maneuvers to guide dispersion of the injectate, inclusive of all imaging guidance and monitoring; multiple incompetent truncal veins (e.g., great saphenous vein, accessory saphenous vein), same leg
36473	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated
36474	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36475	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated
36476	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36478	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated
36479	Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
36482	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (e.g., cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; first vein treated
36483	Endovenous ablation therapy of incompetent vein, extremity, by transcatheter delivery of a chemical adhesive (e.g., cyanoacrylate) remote from the access site, inclusive of all imaging guidance and monitoring, percutaneous; subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)
37500	Vascular endoscopy, surgical, with ligation of perforator veins, subfascial (SEPS)
37700	Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions
37718	Ligation, division, and stripping, short saphenous vein
37722	Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below
37735	Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia
37760	Ligation of perforator veins, subfascial, radical (Linton type), including skin graft, when performed, open,1 leg
37761	Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg
37765	Stab phlebectomy of varicose veins, one extremity; 10-20 stab incisions
37766	Stab phlebectomy of varicose veins, one extremity; more than 20 incisions
37780	Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)
37785	Ligation, division, and/or excision of varicose vein cluster(s), one leg
37799	Unlisted procedure, vascular surgery

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

Clinical Evidence

Endovenous Mechanochemical Ablation

Vähäaho et al. conducted a single-center, randomized controlled trial to evaluate great saphenous vein occlusion (GSV) rates among patients who underwent mechanical occlusion chemically assisted endovenous ablation (MOCA), thermal ablation with endovenous laser (EVLA) or radiofrequency ablation (RFA). The primary outcome was the GSV occlusion rate at 1-year and secondary outcomes were quality of life, patient-reported pain during and after treatment, duration of sick leave, and 30-day complications. Target enrollment was set at 160 patients (assumed 5% lost to follow-up) to detect a 20% difference in occluded or absent GSV between the MOCA and thermal ablation groups (α, 5%; power, 80%). All patients were treated in a day surgery unit, all procedures were done under ultrasound guidance and during the procedure, if patients experienced pain, they were given propofol or fentanyl. A total of 132 patients participated in the study. The first publication (Vähäaho 2019) reported outcomes up to 1 year after treatment. The final analytic sample consisted of 117 patients: 55 patients who were randomized to MOCA, 33 to EVLA and 29 to RFA. The authors concluded that the 1-year GSV occlusion rate for EVLA and RFA were higher than MOCA, while QOL was similar between the treatment methods. The second publication (Vähäaho 2020) reported outcomes up to 3 years after treatment. For this analysis, the final analytic sample consisted of 106 patients: 50 patients who were randomized to MOCA, 31 to EVLA and 25 to RFA. At 3 years, the occlusion rate was significantly lower with MOCA than with either EVLA or RFA (82% vs 100%; p=0.005). Quality of life was similar between the groups. In the MOCA group, GSVs that were larger than 7 mm in diameter preoperatively were more likely to recanalize during the follow-up period. The partial recanalizations of proximal GSV observed at 1 year progressed during the follow-up. The authors concluded that MOCA is a feasible treatment option in an outpatient setting, but its technical success rates are inferior compared with endovenous thermal ablation. Its use in large-caliber veins should be considered carefully. Study limitations include: 1) that the study failed to reach its targeted number of participants; 2) patients, surgeons and follow-up assessors were not blinded to the type of treatment that was given; and 3) medications given during treatment or concomitant phlebectomies may have affected the reliability of the pain scores. Additional randomized trials with larger sample sizes and longer follow-up are still need to evaluate the efficacy and safety of MOCA in the treatment of saphenous vein insuffiency.

Holewijn et al. (2019) conducted a multi-center, randomized controlled trial comparing mechanical occlusion chemically assisted endovenous ablation (MOCA) and radiofrequency ablation (RFA) in the treatment of primary great saphenous vein incompetence. The primary endpoints were pain at 2 weeks after treatment and anatomic success at 1 year after treatment. Secondary endpoints included disease-specific and general health-related quality of life (HRQoL). Sample size calculations were performed and target enrollment was set at 230 patients in each arm (assumed 10% lost to follow-up; α, 5%; power, 80%). A total of 209 patients were treated (105 in the MOCA group and 104 in the RFA group). During the 14 days after treatment, median pain scores were lower in the MOCA group compared with the RFA group (0.2 vs 0.5 p=0.010). At 30 days after treatment, similar complication numbers (MOCA, n=62; RFA, n=63) and HRQoL scores (Aberdeen Varicose Vein Questionnaire: MOCA, 8.9; RFA, 7.6; p=0.233) were observed. Hyperpigmentation was reported in seven patients in the MOCA group and in two patients in the RFA group (p=0.038). The MOCA group had four complete failures (3.8%) compared with none in the RFA group (p=0.045). Median 30-day Venous Clinical Severity Score (VCSS) was significantly lower at 30 days after MOCA vs. RFA (1.0 vs 2.0 p=0.001), although VCSS was comparable at baseline. The 1- and 2- year anatomic success rates were lower after MOCA (83.5% and 80.0%) compared with RFA (94.2% and 88.3%; p=0.025 and 0.066). After 2 years of follow-up, no differences were observed in the number of complete failures. At 1 year and 2 years after treatment, there were no differences in clinical

success rates or HRQoL scores between the treatment groups. There were two patients with cardiac events: ventricular fibrillation (1 year, MOCA) and unstable angina (2 years, RFA), and one patient with a deep venous thrombosis (1 year, RFA). The authors concluded that in the short term, unilateral treatment with MOCA resulted in less postoperative pain but more hyperpigmentation compared with RFA, and there were more anatomic failures reported after MOCA, but both techniques were associated with similar clinical outcomes at 1 year and 2 years after treatment. Study limitations include: 1) that the study failed to reach its targeted number of participants as it was terminated early; 2) not all questionnaires were fully completed; and 3) the use of self-reported data, which may contain sources of bias.

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

Witte et al. (2017) conducted a systematic review and meta-analysis of MOCA of saphenous veins using the ClariVein to report on the anatomical, technical, and clinical success. The literature search identified 759 records, of which 13 were included, describing 10 unique cohorts. A total of 1521 veins (1267 great saphenous vein and 254 small saphenous vein) were included, with cohort sizes ranging from 30 to 570 veins. The pooled anatomical success rate after short-term follow up was 92% (95% CI 90-94%) (n = 1314 veins). After 6 and 12 months these numbers were 92% (95% CI 88-95%) (n = 284) and 91% (95% CI 86-94%) (n = 228), respectively. The long-term anatomical success rates at 2 and 3 years were 91% (95% CI 85-95%) (n = 136) and 87% (95% CI 75-94%) (n = 48), respectively. Major complications and especially nerve injury were very rare (≤ 0.2%). All studies were of moderate or good quality using the MINORS scoring scale. The authors concluded that MOCA using the ClariVein in combination with liquid sclerosant is associated with an anatomical success rate ranging from 87% to 92% and good clinical success. However, they reported that no randomized controlled trials are available studying the anatomical success after MOCA compared to the endothermal ablation.

Kim et al. (2017) evaluated whether early efficacy in endovenous mechanochemical ablation (MOCA) is maintained at 24 months. Patients with reflux in the great saphenous vein involving the sapheno-femoral junction and no previous venous interventions were included. The occlusion rate of treated veins was assessed with duplex ultrasound. Patient clinical improvement was assessed by Clinical-Etiology-Anatomy-Pathophysiology (CEAP) class and venous clinical severity score. Of the initial 126 patients, there were 65 patients with 24 month follow-up. Of these 65 patients, 70% were female, with a mean age of 70 ± 14 years and an average BMI of 30.5 ± 6. The mean great saphenous vein diameter in the upper thigh was 7.6 mm and the mean treatment length was 39 cm. Adjunctive treatment of the varicosities was performed in 14% of patients during the procedure. Closure rates were 100% at one week, 98% at three months, 95% at 12 months, and 92% at 24 months. There was one patient with complete and four with partial recanalization ranging from 7 to 12 cm (mean length 9 cm). There was significant improvement in CEAP and venous clinical severity score (P < .001) for all time intervals. Early high occlusion rate with mechanochemical ablation is associated with significant clinical improvement which is maintained at 24 months, which according to the authors, is suggestive of a good option for the treatment of great saphenous vein incompetence. Longer-term outcomes are needed to evaluate MOCA's efficacy.

Witte et al. (2017) reported midterm results of MOCA for treating great saphenous vein (GSV) insufficiency. In a 1-year period, 85 consecutive patients undergoing MOCA with polidocanol in 104 limbs were enrolled in a prospective registry. The patients were evaluated at baseline and during follow-up (4 weeks and 1, 2, and 3 years) using duplex ultrasound, the CEAP (clinical, etiologic, anatomic and pathophysiologic) classification, the Venous Clinical Severity Score (VCSS), the RAND Short Form 36-Item Health Survey (RAND-SF36), and the Aberdeen Varicose Vein Questionnaire (AVVQ). Primary outcome measures were clinical and anatomic success. Secondary outcome measures included general and disease-specific quality of life and re-interventions. After a median follow-up of 36 months (interquartile range 12.5, 46.3), recanalization occurred in 15 (15%) of 102

successfully treated vein segments. Anatomic success was 92%, 90%, and 87% after 1, 2, and 3 years, respectively. The VCSS improved at all time intervals compared to the preprocedure median. The clinical success at 3 years was 83%. The AVVQ and RAND-SF36 scores showed an improvement at all time intervals compared to baseline values. Between 12 and 36 months, however, a significant deterioration was observed in VCSS, which was accompanied by worsening of disease-specific and general quality of life. Although the authors concluded that MOCA demonstrated to be an effective treatment modality for GSV insufficiency at midterm follow-up, clinical results seemed to drop over time.

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

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

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

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

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

In a pilot study, Van Eekeren et al. (2011) evaluated the feasibility and safety of endovenous MOCA for the treatment of great saphenous vein (GSV) incompetence. Thirty limbs in 25 patients (18 women; mean age 52 years) with GSV incompetence were

treated with the ClariVein® device. Initial technical success, complications, patient satisfaction and classification by venous clinical severity score (VCSS) were assessed 6 weeks after the treatment. Initial technical success of MOCA was 100%. There were no major adverse events. Duplex ultrasonography at 6 weeks showed 26 (87%) of 30 veins were completely occluded. Three veins showed partial recanalization in the proximal and distal GSV. One patient had full segment recanalization and was successfully retreated. The VCSS significantly improved at 6 weeks. Patient satisfaction was high, with a median satisfaction of 8.8 on a 0-10 scale. The authors concluded that endovenous MOCA is feasible and safe in the treatment of GSV incompetence. Larger studies with a prolonged follow-up are indicated to prove the efficacy of this technique.

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

Endovascular Embolization with Cyanoacrylate-Based Adhesive

A Hayes report, Cyanoacrylate Embolization (VenaSeal Closure System) for the Treatment of Varicose Veins, evaluated 7 clinical studies on the efficacy and safety of cyanoacrylate embolization with the VenaSeal Closure System. The evidence included 1 randomized controlled trial, 1 cohort study, 1 case series and 4 pre-post studies. The conclusion states that this low-quality body of evidence suggests that the VenaSeal Closure System may result in reduced symptom severity, improved quality of life and similar occlusion rates when compared with radiofrequency ablation however, substantial uncertainly remains regarding its effectiveness due to the lack of well-designed comparative studies (2020).

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

The VenaSeal Sapheon Closure System Pivotal Study (VeClose) is a multi-center RCT that compared cyanoacrylate closure (CAC) to RFA for the treatment of incompetent great saphenous veins. In this trial, 222 subjects with symptomatic GSV incompetence were randomly assigned to receive either CAC (n=108) with the VenaSeal Sapheon Closure System or RFA (n=114). The primary endpoint was closure of the target vein at month 3, as assessed by duplex ultrasound. To determine non-inferiority of CAE to RFA, the investigators used a predetermined margin of 10%. Secondary endpoints included subject-rated pain experienced during the procedure (i.e., pain experienced after vein access but before all treatment/access catheters were removed), investigator-rated ecchymosis at day 3, adverse events, and details of adjunctive procedures. Patient follow-up visits were on day 3 and at months 1, 3, 6, 12, 24, and 36. For the extension study, patients who were successfully contacted and were interested in participation provided written informed consent for the 60-month follow-up visit. Assessments tools included the Venous Clinical Severity Score (VCSS), Aberdeen Varicose Vein Questionnaire (AVVQ) and EuroQol-Five Dimension (EQ-5D) quality of life survey. This trial has generated multiple publications that reported outcomes with various follow-up periods e.g., 3 months (Morrison, 2015), 12 months (Morrison, 2016) 24 months (Gibson, 2018) and 36 months (Morrison, 2019), as well as a publication with results of a roll-in phase analysis, which included 20 additional patients treated with CAC (Kolluri, 2016).

Morrison et. al. (2020) reported 60-month outcomes from the VeClose trial. A total of 89 (40%) patients of the 220 patients enrolled in the original study completed the 60-month visit. Of those, 47 patients were from the CAC group, 33 patients were from the RFA group, and 9 patients were from the roll-in CAC group. No new recanalization events were observed in the groups between 36 and 60 months of follow-up. At 60 months, Kaplan-Meier estimates for freedom from recanalization in the randomized CAC and RFA groups were 91.4% and 85.2%, respectively, demonstrating noninferiority of CAC compared with RFA. Both groups demonstrated sustained improvements in EQ-5D and quality of life measures through 60 months. 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 are presently at least two CEAP clinical classes lower than at baseline. No long-term device- or procedure-related serious AEs occurred in either group between 36- and 60-month follow-up. The authors concluded that CAC and RFA were effective in achieving complete target vein closure of the GSV at long-term follow-up, with CAC demonstrating continued noninferiority to RFA. CAC was also associated with sustained improvements in symptoms and quality of life, lower CEAP class, and high level of patient satisfaction without serious AEs between 36 and 60 months. Limitations of this study include that the physicians, patients and outcomes assessors could not be blinded to the intervention

received and the small sample size i.e., 40% of the original study population. Additional prospective clinical trials are needed to assess the efficacy and safety of CAC.

Morrison et al. (2019) reported 36-month outcomes from the VeClose trial. Of 222 randomized patients, 146 completed the 36-month follow-up, which included 72 patients from the CAC group and 74 patients from the RFA group. The 36-month great saphenous vein closure rate was 94.4% for the cyanoacrylate closure group and 91.9% for the radiofrequency ablation group. Stable improvement in symptoms and quality of life was observed in both groups. Adverse event rates between the 24- and 36-month visits were similar between the groups as were serious adverse events which were infrequent and judged unrelated to either the device or the procedure in both groups. In the authors' opinion, the results of this trial continue to demonstrate the safety and efficacy of cyanoacrylate closure for the treatment of great saphenous vein incompetence with great saphenous vein closure rate at 36 months similar to that of radiofrequency ablation. Follow-up of the patient cohorts post-procedure will continue up to 60 months. This study was also included in the Hayes report (2020).

Gibson et al. (2018a) reported 24-month outcomes from the VeClose trial. Of 222 randomized patients, 171 completed the 24-month follow-up, which included 87 patients from the CAC group and 84 patients from the RFA group. The 24-month great saphenous vein closure rate was 95.3% in the CAC group and 94.0% in the RFA group, demonstrating continued noninferiority of CAC compared with RFA (P = .0034). Symptoms and quality of life improved similarly in both groups. No clinically significant device- or procedure-related late adverse events were reported. The authors concluded that both CAC and RFA were effective in closure of the target GSV, resulting in similar and significant improvements in the patient's quality of life through 24 months, suggesting that CAC of the GSV is safe and durable out to 2 years. Longer-term outcomes from randomized controlled trials are needed. This study was also included in the Hayes report (2020).

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 postprocedure compression stockings. Concomitant procedures were not allowed as part of the original study protocol. Treating physicians predicted the type and nature of any concomitant procedures that they would usually perform at the time of ablation, if not limited by the constraints of the study. Evaluations were performed at one week, one and three months and included duplex ultrasound, numeric pain rating scale, revised venous clinical severity score, the Aberdeen Varicose Vein Questionnaire, and time to return to work and normal activities. At the three-month visit, the need for and type of adjunctive procedures were recorded. Complete closure at three months was achieved in 70 (99%) of the treated veins (48 great saphenous veins, 14 accessory saphenous veins, eight small saphenous veins). Revised venous clinical severity score improved from 6.4 ± 2.2 to 1.8 ± 1.5 (P < .001) and Aberdeen Varicose Vein Questionnaire from 17.3 ± 7.9 to 6.5 ± 7.2 (P < .0001). Sixty-six percent of patients underwent tributary treatment at three months. The percentage of patients who required adjunctive treatments at three months was lower than had been predicted by the treating physicians (65% versus 96%, p=.0002). The authors reported that closure rates were high in the absence of the use of compression stockings or side branch treatment. Improvement in quality of life 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. This study was also included in the Hayes report (2020).

Eroglu and Yasim (2018) conducted an RCT to compare early and two-year results for N-butyl cyanoacrylate (NBCA), radiofrequency ablation (RFA), and endovenous laser ablation (EVLA) in the treatment of varicose veins. The primary endpoint was the occlusion rate, and secondary endpoints were incidence of complications, and patient satisfaction, including freedom from pain during and after the procedure, complications observed, time to return-to-work and change in VCSS scores. A total of 525 patients were randomized (175 patients in each treatment arm) and 456 patients (NBCA, n=168; RFA, n=149; and EVLA, n=139) had evaluable results i.e., post-procedural ultrasounds and assessments completed at 2 days, and 6, 12 and 24 months. Occlusion rates were similar at 6, 12, and 24 months (6 months [NBCA 98.1%, RFA 94.1%, and EVLA 95.1%, p=0.14], 1 year [NBCA 94.7%, RFA 92.5%, and EVLA 94.2%, p=0.72], 2 years [NBCA 92.6%, RFA 90.9%, and EVLA 91.5%, p=0.89]). Peri-procedural pain was significantly lower after NBCA (p<0.001) but complication rates (DVT, bleeding, and phlebitis) were similar. Time to return-to-work was shortest after NBCA (NBCA 1.04 days, RFA 1.56 days and EVLA 1.31 days (p<0.001) with 95% (NBCA), 50% (RFA) and 75% (EVLA) of patients returning to work on Day 1. Pre-procedural venous clinical severity scores (VCSSs) were the same in all groups. A decrease was observed in VCSS values in all groups at 6 months, and this persisted at 1 and 2 years. However, VCSS scores at 6 months and 2 years were significantly lower in the NBCA group (p<0.001). Foam sclerotherapy was subsequently applied to varicose tributaries in 18 patients from all groups. The authors concluded that no differences were observed in occlusion rates between the three modalities, but NBCA appeared superior with respect to peri-

procedural pain, return-to-work and decreased VCSS. Limitations of this study include that the individuals who performed the procedures were also those who completed the evaluations, the number of patients lost to follow-up varied between the treatment arms, and the short follow-up period. Additional multi-center randomized trials with longer follow-up are needed to further evaluate NBCA in the treatment of varicose veins.

Morrison et al. (2017) reported 12-month outcomes from the VeClose trail. Of 222 randomized patients, a 12-month follow-up was obtained for 192 (95 CAC and 97 RFA; total follow-up rate, 192/222 [86.5%]). By month 12, the complete occlusion rate was nearly identical in both groups (97.2% in the CAC group and 97.0% in the RFA group). Twelve-month freedom from recanalization was similar in the CAC and RFA groups, although there was a trend toward greater freedom from recanalization in the CAC group (P = .08). The authors reported that symptoms and quality of life improved equally in both groups. This study was also included in the Hayes report (2020).

Morrison et al. (2015) reported 3-month outcomes from the VeClose trial. 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). After discharge, subjects returned to the clinic on day 3 and again at months 1 and 3. The study's primary end point was closure of the target vein at month 3 as assessed by duplex ultrasound and adjudicated by an independent vascular ultrasound core laboratory. Statistical testing focused on showing noninferiority with a 10% delta conditionally followed by superiority testing. No adjunctive procedures such as phlebectomy and US foam sclerotherapy were allowed until after the month 3 visit. Fewer patients required phlebectomy than had been predicted, and fewer than predicted incisions were also required. The 3-month closure rates were 99% for VenaSeal and 96% for RFA. The authors concluded that cyanoacrylate ablation was proven to be noninferior to RFA for the treatment of incompetent GSVs at month 3 after the procedure. Both treatment methods showed good safety profiles. The authors also note that cyanoacrylate ablation does not require tumescent anesthesia and is associated with less postprocedure ecchymosis. Further studies will be needed to confirm successful closure as well as to demonstrate other advantages of the VenaSeal® procedure, such as lack of necessity for post-procedural compression and any additional benefits of this non-tumescent technique. This study was also included in the Hayes report (2020).

Gibson and Ferris (2017) reported results of a prospective case series study (the WAVES study) of cyanoacrylate closure for the treatment of great saphenous veins, small saphenous veins, and/or accessory saphenous veins up to 20 mm in diameter (n=50). Compression stockings post-procedure were not utilized. Patients returned at 1 week and 1 month for follow-up. All treated veins (48 great saphenous vein, 14 accessory saphenous veins, and 8 small saphenous veins) had complete closure by duplex ultrasound at seven days and one month. Mean time to return to work and normal activities was 0.2 ± 1.1 and 2.4 ± 4.1 days, respectively. The revised venous clinical severity score was improved to 1.8 ± 1.4 ($p < .001$) and Aberdeen Varicose Vein Questionnaire score to 8.9 ± 6.6 ($p < .001$) at one month. Phlebitis in the treatment area or side branches occurred in 10 subjects (20%) and completely resolved in all but one subject (2%) by one month. The authors concluded that cyanoacrylate closure is safe and effective for the treatment of one or more incompetent saphenous or accessory saphenous veins, closure rates were high even in the absence of the use of compression stockings or side branch treatment. Time back to work or normal activities was short and improvements in venous severity scores and QOL were in the authors' opinion significant, comparing favorably with alternative treatment methods. Randomized controlled trials with a larger patient population and longer follow-up periods are needed to validate findings. This study was also included in the Hayes report (2020).

Bozkurt and Yilmaz (2016) conducted a prospective comparative study of 310 adult subjects who were treated with cyanoacrylate ablation or endovenous laser ablation. The primary endpoint of this study was complete occlusion of the great saphenous vein. One, three, and 12 months closure rates were 87.1, 91.7, and 92.2% for endovenous laser ablation and 96.7, 96.6, and 95.8% for cyanoacrylate ablation groups. Closure rate at first month was significantly better in cyanoacrylate ablation group (<0.001). Although there is a trend of better closure rates in cyanoacrylate ablation patients, this difference did not reach to the statistical difference at sixth and 12th month ($p = 0.127$ and 0.138, respectively). The authors concluded that the efficacy and safety analysis shows that cyanoacrylate ablation is a safe, simple method which can be recommended as an effective endovenous ablation technique. However, follow-up data of greater than one year is needed to clarify the future role of cyanoacrylate ablation for the treatment incompetent great saphenous veins. This study was also included in the Hayes report (2019).

Almeida et al. (2015) evaluated the safety and effectiveness of endovenous cyanoacrylate-based embolization of incompetent great saphenous veins 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 great saphenous vein was confirmed by duplex ultrasound in all

patients except for one complete and two partial recanalizations observed at, 1, 3 and 6 months of follow-up, respectively. Kaplan-Meier analysis yielded an occlusion rate of 92.0% (95% CI 0.836-1.0) at 24 months follow-up. Venous Clinical Severity Score improved in all patients from a mean of 6.1 ± 2.7 at baseline to 1.3 ± 1.1, 1.5 ± 1.4 and 2.7 ± 2.5 at 6, 12 and 24 months, respectively (p < .0001). Edema improved in 89% of legs (n = 34) at 48 hours follow-up. At baseline, only 13% were free from pain. At 6, 12 and 24 months, 84%, 78% and 64% were free from leg pain, respectively. Small sample size is a limitation to this study. This study was also included in the Hayes report (2019).

A prospective multicenter case series study was conducted on 78 patients with GSV reflux using cyanoacrylate embolization (Proebstle et al., 2015). Clinical examination, quality of life assessment and duplex ultrasound were performed at 2 days, 1, 3, 6, and 12 months. 68 (97.1%) were available for 12-month follow-up. Two-day follow-up showed one proximal and one distal partial recanalization. Three additional proximal recanalizations were observed at 3-month (n = 2) and 6-month (n = 1) follow-up. Cumulative 12-month survival free from recanalization was 92.9% (95% confidence interval, 87.0%-99.1%). Mean (standard deviation) Venous Clinical Severity Score improved from 4.3 Â± 2.3 at baseline to 1.1 Â± 1.3 at 12 months. Aberdeen Varicose Vein Questionnaire score showed an improvement from 16.3 at baseline to 6.7 at 12 months (P < .0001). Side effects were generally mild; a phlebitic reaction occurred in eight cases (11.4%) with a median duration of 6.5 days (range, 2-12 days). Pain without a phlebitic reaction was observed in five patients (8.6%) for a median duration of 1 day (range, 0 -12 days). No serious adverse event occurred. Paresthesia was not observed. The authors concluded that endovenous CA embolization of refluxing GSVs is safe and effective without the use of tumescent anesthesia or compression stockings. Additional studies are needed to validate the effectiveness of cyanoacrylate embolization. This study was also included in the Hayes report (2020).

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.

Endovenous Foam Sclerotherapy

In a 5-year follow-up of a randomized clinical trial comparing open surgery, ultrasound guided foam sclerotherapy (UGFS) and endovenous laser ablation (EVLA) for great saphenous varicose veins, Vähäaho et al. (2018) evaluated long-term results of surgery, EVLA and UGFS in the treatment of GSV reflux. Patients with symptomatic GSV reflux were randomized to undergo either open surgery, EVLA or UGFS. The main outcome measure was the occlusion rate of the GSV at 5 years after operation. The study included 196 patients; of these, 166 (84·7 per cent) participated in the 5-year follow-up. At 5 years, the GSV occlusion rate was 96 (95 per cent c.i. 91 to 100) per cent in the open surgery group, 89 (82 to 98) per cent after EVLA and 51 (38 to 64) per cent after UGFS (P < 0·001). For patients who had received no additional treatment during follow-up, the occlusion rates were 96 per cent (46 of 48), 89 per cent (51 of 57) and 41 per cent (16 of 39) respectively. UGFS without further GSV treatment was successful in only 16 of 59 patients (27 per cent) at 5 years. The authors concluded that UGFS has significantly inferior occlusion rates compared with open surgery or EVLA, and results in additional treatments.

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

Gibson et al. (2017) conducted a randomized, placebo-controlled, multicenter study to evaluate the safety and efficacy of polidocanol endovenous microfoam (1%, Varithena® [polidocanol injectable foam]. Patients (n = 77) with symptomatic, visible varicose veins were randomized to treatment with either Varithena 1% or placebo. Patients were assessed at baseline and weeks 1, 4, 8, and 12 post-treatment. The data showed that Varithena provided greater mean changes from baseline in patient-reported assessments of symptoms (e.g., heaviness, achiness, swelling, throbbing, itching [HASTI®] score 30.7 points vs 16.7 points, p = 0.0009, primary endpoint; and modified Venous Insufficiency Epidemiological and Economic Study-Quality-of-Life/Symptoms [m-VEINES-QOL/Sym; p < 0.001]), physician-assessed VCSS, and physician- and patient-assessed appearance compared with placebo. The HASTI score correlated highly with the modified-VEINES-QOL/Sym and Chronic Venous Insufficiency Questionnaire-2 scores (r = 0.7 to > 0.9, p ≤ 0.001). Adverse events included contusion, incision-site hematoma, and limb discomfort. Venous thrombus adverse events were reported as mild and generally resolved without sequelae. Large randomized controlled trials with longer-term outcomes and comparisons to established treatments for varicose veins are needed to evaluate the clinical utility of this procedure

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

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

In the VANISH-2 trial, Todd et al. (2014) evaluated the efficacy and safety of polidocanol endovenous microfoam in treatment of symptoms and appearance in patients with saphenofemoral junction incompetence due to reflux of the great saphenous vein or major accessory veins. Patients were randomized equally to receive polidocanol endovenous microfoam 0.5%, polidocanol endovenous microfoam 1.0% or placebo. In 232 treated patients, polidocanol endovenous microfoam 0.5% and polidocanol endovenous microfoam 1.0% were superior to placebo, with a larger improvement in symptoms (VVSymQ (-6.01 and-5.06, respectively, versus -2.00; P < 0.0001) and greater improvements in physician and patient assessments of appearance (P < 0.0001). These findings were supported by the results of duplex ultrasound and other clinical measures. Of the 230 polidocanol endovenous microfoam-treated patients (including open-label patients), 60% had an adverse event compared with 39% of placebo; 95% were mild or moderate. The authors concluded that polidocanol endovenous microfoam provided clinically meaningful benefit in treating symptoms and appearance in patients with varicose veins. However, longer-term outcomes with comparisons between PEM and other established treatments for varicose veins are needed to evaluate the clinical utility of this procedure.

Lal et al. (2017) evaluated the relationship between patient-reported symptoms and functional and psychological impact of varicose veins following treatment with polidocanol endovenous microfoam (PEM) 1%. Data were pooled from two randomized

trials on varicose vein treatment. In 221 patients (109 PEM 1%; 112 placebo), PEM 1% was associated with median improvements of 2.5 points and 4.0 points on the m-VEINES-QOL/Sym functional limitations and m-VEINES-QOL/Sym psychological limitations scores, compared to 0 and 1.0 point. Cumulative distribution function curves revealed that 20-30% more patients in the PEM 1% group achieved clinically meaningful functional and psychological improvement versus placebo group. Patients with above-average symptom improvement had better functional and psychological improvement. PEM 1% treatment had higher odds of clinically meaningful functional and psychological improvement. Length of post-procedure follow-up was not provided. Furthermore, this study did not compare endovenous microfoam to established treatement for varicose veins.

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

U.S. Food and Drug Administration (FDA)

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

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

The ClariVein® infusion catheter (Vascular Insights) received FDA approval (K071468) on March 20, 2008. The device is designed to introduce physician-specified medicaments into the peripheral vasculature. See the following website for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf7/K071468.pdf. (Accessed Janaury 7, 2021)

The VenaSeal™ Closure System received the FDA's pre-market approval (PMA) on February 20, 2015 (P140018). The device is indicated for the permanent closure of lower extremity superficial truncal veins, such as the great saphenous vein (GSV), through endovascular embolization with coaptation. VenaSeal is intended for use in adults with clinically symptomatic venous reflux as diagnosed by duplex ultrasound (DUS). See the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140018. (Accessed Janaury 7, 2021)

Varithena (polidocanol injectable foam) (Provensis Ltd.) received FDA approval on November 25, 2013 as a sclerosing agent indicated for the treatment of incompetent great saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous vein system above and below the knee. See the following websites for more information:

- https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/205098Orig1s000ltr.pdf
- https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/205098s000lbl.pdf

(Accessed Janaury 7, 2021)

References

Almeida JI, Javier JJ, Mackay EG, et al. Two-year follow-up of first human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. Phlebology. 2015 Jul;30(6):397-404.

American Medical Association. Current Procedural Terminology: CPT Professional Edition. AMA Press.

Bishawi M, Bernstein R, Boter M, et al. Mechanochemical ablation in patients with chronic venous disease: A prospective multicenter report. Phlebology. 2014 Jul;29(6):397-400.

Boersma D, van Eekeren RR, Werson DA, et al. Mechanochemical endovenous ablation of small saphenous vein insufficiency using the ClariVein® device: one-year results of a prospective series. Eur J Vasc Endovasc Surg. 2013 Mar;45(3):299-303.

Bootun R, Lane T, Dharmarajah B, et al. Intra-procedural pain score in a randomised controlled trial comparing mechanochemical ablation to radiofrequency ablation: The multicentre Venefit™ versus ClariVein® for varicose veins trial. Phlebology. 2016 Feb;31(1):61-5.

Bozkurt AK, Yılmaz MF. A prospective comparison of a new cyanoacrylate glue and laser ablation for the treatment of venous insufficiency. Phlebology. 2016 Mar;31(1 Suppl):106-13.

CPT Assistant. Correct coding of endovascular treatment for low extremity venous incompetency. October 2014.

Elias S, Raines JK. Mechanochemical tumescentless endovenous ablation: final results of the initial clinical trial. Phlebology. 2012 Mar;27(2):67-72.

Eroglu E, Yasim A. A randomised clinical trial comparing n-butyl cyanoacrylate, radiofrequency ablation and endovenous laser ablation for the treatment of superficial venous incompetence: two year follow up results. Eur J Vasc Endovasc Surg. 2018 Oct;56(4):553-560.

Gibson K, Morrison N, Kolluri R, et al. Twenty-four month results from a randomized trial of cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2018a Sep;6(5):606-613.

Gibson K, Minjarez R, Gunderson K, et al. Need for adjunctive procedures following cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of postprocedure compression: Three-month data from a postmarket evaluation of the VenaSeal System (the WAVES Study). Phlebology. 2018b Sep 18:268355518801641.

Gibson K, Kabnick L, Varithena 03 Investigator Group. A multicenter, randomized, placebo-controlled study to evaluate the efficacy and safety of Varithena® (polidocanol endovenous microfoam 1%) for symptomatic, visible varicose veins with saphenofemoral junction incompetence. Phlebology. 2017 Apr;32(3):185-193. Epub 2016 Jul 9.

Gibson K, Ferris B. Cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of post-procedure compression: Initial outcomes of a post-market evaluation of the VenaSeal System (the WAVES Study). Vascular. 2017 Apr;25(2):149-156.

Hayes, Inc. Hayes Health Technology Assessment. Cyanoacrylate Embolization (VenaSeal Closure System) for the Treatment of Varicose Veins. Lansdale, PA: Hayes, Inc.; December 2020.

Hayes, Inc. Hayes Health Technology Brief. Polidocanol endovenous microfoam (Varithena) 1% for treatment of varicose veins. Lansdale, PA: Hayes, Inc.; May 2016. Updated December 2020.

Holewijn S, van Eekeren RRJP, Vahl A, et al. Two-year results of a multicenter randomized controlled trial comparing mechanochemical endovenous ablation to radiofrequency ablation in the treatment of primary great saphenous vein incompetence (MARADONA trial). J Vasc Surg Venous Lymphat Disord. 2019 May;7(3):364-374.

Kim PS, Bishawi M, Draughn D, et al. Mechanochemical ablation for symptomatic great saphenous vein reflux: a two-year follow-up. Phlebology. 2017;32(1):43-48.

King JT, O'Byrne M, Vasquez M, et al. Treatment of truncal incompetence and varicose veins with a single administration of a new polidocanol endovenous microfoam preparation improves symptoms and appearance. Eur J Vasc Endovasc Surg. 2015 Dec;50(6):784-93. Epub 2015 Sep 16.

Kolluri R, Gibson K, Cher D, et al. Roll-in phase analysis of clinical study of cyanoacrylate closure for incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2016 Oct;4(4):407-15.

Lal BK, Mallick R, Wright D. Improvement in patient-reported outcomes of varicose veins following treatment with polidocanol endovenous microfoam. Phlebology. 2017 Jun;32(5):342-354.

Lane T, Bootun R, Dharmarajah B, et al. A multi-centre randomised controlled trial comparing radiofrequency and mechanical occlusion chemically assisted ablation of varicose veins – Final results of the Venefit versus Clarivein for varicose veins trial. Phlebology. 2017 Mar;32(2):89-98.

Lawaetz M, Serup J, Lawaetz B, et al. Comparison of endovenous ablation techniques, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Extended 5-year follow-up of a RCT. Int Angiol. 2017 Jun;36(3):281-288.

Morrison N, Gibson K, McEnroe S, et al. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). J Vasc Surg. 2015 Apr;61(4):985-94.

Morrison N, Gibson K, Vasquez M, et al. Five-year extension study of patients from a randomized clinical trial (VeClose) comparing cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2020 Nov;8(6):978-989.

Morrison N, Gibson K, Vasquez M, et al. VeClose trial 12-month outcomes of cyanoacrylate closure versus radiofrequency ablation for incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2017 May;5(3):321-330.

Morrison N, Kolluri R, Vasquez M, et al. Comparison of cyanoacrylate closure and radiofrequency ablation for the treatment of incompetent great saphenous veins: 36-month outcomes of the VeClose randomized controlled trial. Phlebology. 2018 Nov 7:268355518810259.

National Institute for Health and Care Excellence (NICE). Interventional procedures guidance (IPG557) Endovenous mechanochemical ablation for varicose veins. May 2016.

National Institute for Health and Care Excellence (NICE). Cyanoacrylate glue occlusion for varicose veins. Interventional procedure guidance [IPG670]. March 2020.

National Institute for Health and Care Excellence (NICE). Interventional procedure guidance [IPG 440]. Ultrasound-guided foam sclerotherapy for varicose veins. February 2013.

Proebstle TM, Alm J, Dimitri S, et al. The European multicenter cohort study on cyanoacrylate embolization of refluxing great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2015 Jan;3(1):2-7.

Todd KL 3rd, Wright DI, VANISH-2 Investigator Group. The VANISH-2 study: a randomized, blinded, multicenter study to evaluate the efficacy and safety of polidocanol endovenous microfoam 0.5% and 1.0% compared with placebo for the treatment of saphenofemoral junction incompetence. Phlebology. 2014 Oct;29(9):608-18.

Vähäaho S, Halmesmäki K, Albäck A, et al. Five-year follow-up of a randomized clinical trial comparing open surgery, foam sclerotherapy and endovenous laser ablation for great saphenous varicose veins. Br J Surg. 2018 May;105(6):686-691.

Vähäaho S, Mahmoud O, Halmesmäki K, et al. Randomized clinical trial of mechanochemical and endovenous thermal ablation of great saphenous varicose veins. Br J Surg. 2019 Apr;106(5):548-554.

van Eekeren RR, Boersma D, Konijn V, et al. Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. J Vasc Surg. 2013 Feb;57(2):445-50.

van Eekeren RR, Boersma D, Elias S, et al. Endovenous mechanochemical ablation of great saphenous vein incompetence using the ClariVein device: a safety study. J Endovasc Ther. 2011 Jun;18(3):328-34.

Varithena® website. BTG Interventional Medicine. Available at: https://www.btg-im.com/en-US/Varithena/Home. Accessed December 23, 2019.

Vasquez M, Gasparis AP, Varithena® 017 Investigator Group. A multicenter, randomized, placebo-controlled trial of endovenous thermal ablation with or without polidocanol endovenous microfoam treatment in patients with great saphenous vein incompetence and visible varicosities. Phlebology. 2017 May;32(4):272-281.

VenaSeal™ Closure System website. Medtronic. Available at: http://medtronicendovenous.com/patients/7-2-venaseal-closure-procedure/. Accessed January 7, 2021.

Vun SV, Rashid ST, Blest NC, Spark JI. Lower pain and faster treatment with mechanico-chemical endovenous ablation using ClariVein®. Phlebology. 2015 Dec;30(10):688-92.

Witte ME, Holewijn S, van Eekeren RR, et al. Midterm outcome of mechanochemical endovenous ablation for the treatment of great saphenous vein insufficiency. J Endovasc Ther. 2017 Feb;24(1):149-155. Epub 2016 Oct 15.

Witte ME, Zeebregts CJ, de Borst GJ, et al. Mechanochemical endovenous ablation of saphenous veins using the ClariVein: A systematic review. Phlebology. 2017 Dec;32(10):649-657.

Policy History/Revision Information

Date	Summary of Changes
07/01/2021	**Coverage Rationale** • Replaced references to "InterQual® 2020" with "InterQual® 2021" **Supporting Information** • Archived previous policy version CS117IN.01

Instructions for Use

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