Review Article

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1% polidocanol endovenous microfoam (Varithena™) for the treatment of chronic venous disease: A position statement from the American vein and lymphatic society

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Abstract

Background: A variety of minimally invasive thermal and non-thermal techniques to treat superficial truncal vein reflux have been introduced over the past 2 decades. Among these has been polidocanol endovenous microfoam (PEM, VarithenaTM). This position statement reviews the clinical results of the use of PEM in chronic venous disease as well as those situations where PEM may have distinct advantages over other endovenous modalities.

Method: An expert panel of the American Vein and Lymphatic Society reviewed the literature, focusing on the clinical outcomes and unique advantages associated with the use of PEM.

Result: In vitro, ex vivo, and clinical studies have shown PEM to have greater stability and efficacy than physician compounded foam, while other studies have demonstrated saphenous closure rates and clinical outcomes similar to those achieved with thermal ablation. Despite the benefits across the spectrum of chronic venous disease, PEM may have advantages in minimizing the risk of nerve injury associated with treatment of the below knee reflux, treating venous ulcers, and managing recurrent varicose veins and difficult saphenous anatomy due to tortuosity or intraluminal synechia.

Conclusion: As the only FDA approved foam sclerosant, PEM provides flexibility in treating patients with standard, variant, and recurrent venous anatomy. The American Vein and Lymphatic Society supports PEM as a safe and effective treatment option for the treatment of C2-C6 disease associated with superficial venous reflux.

Keywords

Venous insufficiency, varicose veins, venous ulcer, foam sclerotherapy

Introduction

Over the past 2 decades, the traditional management of symptomatic saphenous vein reflux with high ligation and stripping (HLS) has been supplanted by a variety of office-based percutaneous interventions. Rather than requiring general anesthesia in an operating room setting, these minimally invasive techniques allow outpatient office-based treatment to be performed under local anesthesia, with or without sedation. Thermal ablation of the great saphenous (GSV) vein, using either endovenous laser (EVLA) or radiofrequency (RFA), were among the earliest minimally invasive techniques. Systematic reviews of both randomized controlled and observational studies have demonstrated less post-operative pain and analgesic requirements with the thermal techniques, with 5-year anatomic closure rates comparable to HLS.[1] Thermal techniques have also been associated with a more rapid return to work and usual activities.[2,3] Since the introduction of thermal ablation, a variety of non-thermal techniques, including cyanoacrylate, mechanicochemical (MOCA), and non-compounded microfoam (polidocanol endovenous microfoam – PEM, Varithena™) ablation have been developed. These techniques provide comparable outcomes to thermal ablation without the requirement for tumescent anesthesia, resulting in less intraoperative pain, little risk of nerve injury and minimal skin damage. Depending on the

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expertise of the physician and patient preferences, the multisocietal (American Vein & Lymphatic Society, American Venous Forum, Society for Vascular Surgery) venous guidelines accordingly recommend either thermal or nonthermal techniques for the treatment of symptomatic great saphenous (GRADE 1B), small saphenous (1C), and accessory saphenous (2C) vein reflux.[4] As patient preferences and anatomy vary, having a choice of treatment options is critical in assuring optimal outcomes in individual patients.

Non-compounded foam sclerotherapy (PEM, Varithena™)

Detergent sclerosants have long been used in the treatment of venous disease and foam sclerosants have several advantages over liquid sclerosants in the treatment of larger superficial veins. Liquid sclerosants are rapidly diluted by blood and inactivated by binding to plasma proteins while foam sclerosants displace blood, prolonging contact with the vein wall, disrupting the endothelium, and ultimately leading to sclerosis. Foam sclerosants achieve greater efficiency at a lower sclerosant concentration. In considering foam sclerosants, polidocanol endovenous microfoam (PEM, Varithena™; Boston Scientific, Marlborough, MA), or non-compounded foam, must be distinguished from physician compounded foam (PCF) prepared using a variety of detergent sclerosants, gas mixtures, and foam generating techniques.[5] According to the American Medical Association CPT definition,[6] "compounding is a practice in which a qualified health care professional (e.g. pharmacist, physician) combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient". Varithena™, or PEM, is the only foam sclerosant approved by the United States Food and Drug Administration (FDA) for the treatment of varicose veins and differs biologically and clinically from PCF. Varithena™ uses an automated proprietary foam-generating canister to produce a virtually nitrogen-free (<0.8%) 1% polidocanol foam with a 65:35 ratio of O_2 to CO_2.[5,7]

The ideal foam sclerosant should have adequate cohesiveness to displace blood rather than mixing with it and should be sufficiently stable to maintain its biologic effect until endothelial cell death occurs but sufficiently transient to minimize complications.[7] In vitro and ex vivo studies have demonstrated significant differences between PEM and PCF. Dwell time, a measure of foam cohesiveness and a reflection of the time foam is in contact with the vein wall is longer for PEM than for PCF.[5] In vitro studies have similarly demonstrated PEM to be substantially more stable than PCF and to have significantly great efficacy as measured by endothelial cell detachment in a human umbilical vein endothelial cell (HUVEC) model.[7] Ex vivo studies using umbilical vein segments similarly demonstrated greater endothelial disruption with PEM. Consistent with the in vitro and ex vivo studies, a network meta-analysis has shown the rate of saphenous closure at a median of 12 months to be almost 3 times more likely (OR, 2.91; 95% CI 1.58 – 5.37; $p < .01$) with PEM than with PCF.[8]

Although both liquid and foam sclerosants have been associated with neurologic complications including cerebrovascular accidents (CVA), transient ischemic attacks (TIA), visual / speech disturbances, and headaches, these events appear to be more common with foam sclerosants. A systematic review of cohort studies and randomized trials found no reported CVAs after sclerotherapy, although the incidence of TIA or amaurosis fugax, visual disturbances, and headaches was 0.06%, 0.78%, and 0.7% respectively.[9] However, the review did identify several case reports of TIA / CVA. Similarly, a review of the U.S. Food and Drug Administration Adverse Events Reporting System database and MEDLINE identified 23 neurologic or cardiac adverse events (NCAEs) associated with leg vein sclerotherapy, 10 of which documented the use of physician compounded foam.[10] Thirteen of these events were classified as a CVA/TIA. The prescribing information for both Asclera® (polidocanol - https://asclera.com/wp-content/uploads/2023/10/Asclera-Prescribing-info-EN_Feb2-2022.pdf) and Sotradecol® (sodium tetradecyl sulfate - https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f1756c28-dcd2-4b49-be62-07ca20682018) accordingly recommend that sclerosants foamed with room air be avoided. A number of potential mechanisms for these events have been suggested including large bubble size and the insolubility of nitrogen in air-based foams. Based upon these potential mechanisms, PEM, which is virtually (≤0.8%) nitrogen free with a uniform bubble size <500 μm[5], should minimize such complications. Consistent with these theoretical considerations, an intensive investigation of 61 patients with known right to left shunts identified no new neurologic symptoms or MRI abnormalities after treatment with PEM.[11] The absence of significant neurologic side effects has subsequently been confirmed in clinical trials and observational studies.

Clinical results - pivotal (phase 3) trials

VANISH-1

This multicenter, parallel group study was designed to determine if a single administration of ≤15 mL of pharmaceutical grade PEM could alleviate symptoms and improve the 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.[12] Two hundred seventy-nine patients were randomized to placebo (agitated saline, $n = 56$), PEM 0.125% (control, $n = 57$), PEM 0.5% ($n = 51$),

PEM 1.0% ($n = 52$), or PEM 2.0% ($n = 63$). Mean baseline GSV diameter was 7.63 mm (range 1.5 – 25.9 mm). The primary endpoint was improvement in patient-reported venous symptoms between baseline and week 8 as measured by the 7-day average VVSymQ score (patient reported symptoms of *H*eaviness, *A*chiness, *S*welling, *T*hrobbing, and *I*tching - *HASTI*). At 8 weeks, average VVSymQ improved by 5.44 among patients in the pooled PEM (0.5%, 1%, and 2%) group in comparison to only 2.13 in the placebo group ($p < .0001$). Duplex response at 8 weeks, defined as the elimination of saphenofemoral junction (SFJ) reflux and/or complete occlusion of the target vein, was 74.5% in the pooled PEM group versus 5.4% in the placebo group ($p < .001$). There was a significant ($p < .001$) dose-response trend between PEM concentrations and for the commercially available preparation (1%), duplex response was 80.4%. Thirty-four percent of patients did undergo a second treatment after 8 weeks per the predefined protocol. In comparison to placebo, the pooled PEM group also demonstrated significant improvements in physician and patient assessed appearance of varicose veins ($p < .001$), venous clinical severity score (VCSS; $p < .001$), and Venous Insufficiency Epidemiologic and Economic Study-Quality of Life / Symptoms score (VEINES-QOL/Sym; $p < .001$). With respect to safety, most adverse events were mild and resolved without sequelae. The most common adverse events were superficial thrombophlebitis (7.7% in PEM 1%), extremity pain (19.2%), and injection site hematoma (7.7%). Venous thrombosis occurred in 27/223 (12.1%) PEM-treated patients. Among these 27 events, 15 (55.6%) were saphenofemoral thrombus extensions, 5 (18.5%) were proximal deep venous thromboses (DVT), 4 (17.6%) were distal DVTs, and 3 (11%) were isolated gastrocnemial-soleal thromboses. The fate of these thrombi was clinically benign – all were detected by protocol-required ultrasound, 88% were asymptomatic, and there were no clinically confirmed pulmonary emboli (PE). All resolved within 100 days (median 21 days), independent of treatment, which was not pre-specified in the protocol.

VANISH-2

This Phase 3 pivotal study randomized 230 patients with saphenofemoral junction incompetence due to reflux of the great saphenous vein or major accessory veins to polidocanol endovenous microfoam 1.0%, 0.5%, 0.125% (control) or placebo. Mean GSV diameter was 8.7 (range 3.1 – 19.4) mm.[13] The protocol allowed retreatment at 1 week and overall patients received an average of 1.4 blinded treatments. Clinically meaningful improvement in VVSymQ, the primary endpoint, was seen in 80.5% of pooled PEM (0.5% and 1.0%) patients in comparison to 21.2% of those receiving placebo ($p < .0001$). Clinically meaningful improvements in appearance, as assessed by both expert clinicians and patients, as well as VCSS and VEINES-QOL were also significantly ($p < .0001$) more common in patients treated with PEM in comparison to placebo. As a tertiary outcome, duplex ultrasound response, again defined as the elimination of SFJ reflux and/ or complete target vein occlusion occurred in 84.7% of pooled PEM-treated patients in comparison to 1.8% of those treated with placebo. Thrombotic events occurred in 24 patients. All were detected by protocol driven duplex ultrasound and most (77%) were asymptomatic. These included saphenofemoral thrombus extension in nine patients (3.9% of PEM treated patients), proximal DVT in 6 (2.6%), distal DVT in 7 (3%), and gastrocnemial thrombus in 2 (0.9%). Regardless of treatment, most were clinically inconsequential and there were no pulmonary emboli. Among the 58 patients treated with 1% PEM and followed for 1 year, there were no pulmonary emboli and no patient developed post-thrombotic sequelae.[14]

Both pivotal trials demonstrated ≤15 mL of the commercially available 1.0% polidocanol endovenous microfoam administered from a mid-thigh puncture to be an effective and comprehensive minimally invasive treatment for patients with a broad spectrum of venous disease (CEAP class C2 to C6) and GSV diameters up to 25.9 mm. It provided clinically meaningful benefits in treating both symptoms and appearance and was associated with manageable side effects.

Clinical results - post-market studies

In addition to the two pivotal trials, a Pub Med search using "polidocanol endovenous microfoam [Title/Abstract]) OR (Varithena [Title/Abstract])" returned 30 publications, including six clinical trials, which address the clinical use of PEM.[14–19] Highlights of these publications are discussed below.

The 56 patients randomized to 1% PEM (FDA approved concentration – Varithena™) in the VANISH-2 trial were followed clinically and with ultrasound 1 year after treatment.[14] Forty-three percent and 10.3% of patients received additional treatment with 1% PEM at 1 and 2 weeks after completion of the initial 8-week study. Symptoms measured by the VVSymQ continued to improve over time with a VVSymQ score ≤3 in 64% and 85% at 8 weeks and 1 year respectively. At 1 year, 86% and 87.7% of patients had a clinically meaningful improvement in symptoms and patient-assessed appearance respectively. Duplex response, defined as the elimination of SFJ reflux and/or complete occlusion of the target vein slightly decreased from 89% at 8 weeks to 73% at 1 year. However, sustained improvement in symptoms was seen even in duplex non-responders. Notably, no new thrombotic events, pulmonary emboli or post-thrombotic syndrome were identified during follow-up.

Although physician-compounded foams have been included in randomized clinical trials, no such trials have directly compared PEM, which as above is distinctly different from PCF, to other treatment modalities. However, several case series provide evidence of comparable efficacy for PEM and thermal ablation. In a retrospective study designed primarily to look at treatment results in 131,268 Medicare and non-Medicare eligible patients, outcomes were also evaluated among those treated with thermal ablation versus Varithena™.[20] At 6 months, there were no differences in the revised Venous Clinical Severity Score (rVCSS) or Chronic Venous Insufficiency Questionnaire (CIVIQ) among those treated with thermal ablation alone or Varithena™ alone. In another retrospective analysis, outcomes in 550 PEM treated patients were compared to those in 520 patients treated with EVLA.[21] At a mean follow-up of 43 ± 13 months (EVLA) and 57 ± 18 months (PEM), target vein closure was achieved in 92.8% and 93.5% of limbs respectively. A second treatment was required in 17.1% of PEM treated patients for symptomatic residual veins below the knee. Thrombotic complications in the two groups were comparable, asymptomatic DVT in 0.4% and 0.8% and ablation-related thrombus extension (ARTE) in one and two patients treated with PEM and EVLA respectively. Another series[22] compared clinical and ultrasound outcomes in 200 consecutive patients with GSV or anterior saphenous (ASV) reflux treated with either RFA or PEM. Closure rates at 48 – 72 hours, defined as occlusion to within 10 cm of the saphenofemoral junction, were ≥90% in both groups, although slightly higher for RFA (100% vs 90%, $p = .005$). Early re-intervention rates for residual symptoms were identical (15%) in the two groups. Symptomatic improvement was also similar in the two groups, 90% for RFA and 89% for PEM. There were no symptomatic DVTs or PEs in either group. Ablation-related thrombus extension occurred in 1% and 4% of RFA and PEM treated patients respectively. A final series[23] compared the efficacy of RFA ($n = 66$) and PEM ($n = 66$) in patients with large diameter (≥8 mm) great, anterior, or small saphenous veins. Early post-procedural (48 – 72 hours) closure rates were comparable - 99% after RFA and 94% after PEM. After a mean follow-up of 62 – 95 days, symptomatic improvement was seen in 92% and 91% and ulcer healing in 83% and 79% of limbs after RFA and PEM respectively. No symptomatic DVTs or PEs were identified, and ultrasound detected ARTE was seen in 3.0% of RFA treated limbs in comparison to 6.1% of PEM treated limbs ($p = .36$).

Lastly, a network meta-analysis has compared PEM to thermal ablation in 13 studies including 233,801 patients.[8] Vein closure at a median of 12 months was not statistically different among patients treated with PEM in comparison to those treated with thermal ablation (OR 0.65; 95% CI 0.36 – 1.18; $p = .16$). This equivalence was maintained out to a median follow-up of 48 months. Rates of post-procedural DVT were also equivalent among patients treated with PEM and thermal ablation.

Clinical results – special considerations

Although PEM provides meaningful patient benefit across the spectrum of chronic venous disease related to varicose veins, it may provide additional value over other treatment modalities in specific circumstances as discussed below.

The below knee great saphenous vein

Since the widespread adoption of HLS, most venous specialists have limited truncal interventions, including thermal ablation, to the above knee GSV to avoid saphenous nerve injury. However, the incidence of persistent below knee saphenous reflux after above knee ablation has been reported to be 44%–91%.[24,25]

Sussman[24] evaluated the risk of below knee recurrence after above knee intervention in a systematic review including 15 studies. Below knee recurrence was found in 29.9% of patients after HLS in comparison to 15.7% 1 year after EVLA. Among five randomized trials directly comparing HLS and EVLA, below knee recurrence was not significantly different between the two interventions (8.5% vs 6.8% respectively). However, among the two randomized trials that directly compared above knee EVLA to above + below knee EVLA, treatment of the below knee segment did significantly reduce the risk of recurrence (OR 0.19, 0.08 – 0.47). The authors concluded that although treatment of the above knee segment may be sufficient for patients with C2 disease, C4 – C6 disease justifies more aggressive treatment of the above and below knee GSV.

Although saphenous nerve injury has been reported in 16% of patients after HLS, it appears to be substantially less common after thermal ablation of the below knee GSV.[24,26] In a meta-analysis of 13 studies including 2245 limbs, EVLA was associated with a 41% risk reduction in the incidence of paresthesia in comparison to HLS (6.73 vs 11.27 %).[27] However, the 3.8% - 6.7% incidence of paresthesias[26] reported after thermal ablation is not inconsequential, and most venous specialists avoid thermal interventions below the knee. The non-thermal modalities, including Varithena™, are invaluable techniques for managing below knee saphenous reflux with minimal risk of nerve injury. In a series of 68 limbs with symptomatic below knee reflux (below knee GSV - 45, small saphenous vein - 23) after above knee ablation or HLS, an early closure rate of 96% was achieved with no saphenous or sural nerve injury.[25] A larger series of 411 patients treated with PEM for symptomatic reflux in either the below-knee GSV (554 procedures) or small saphenous vein (SSV – 42 procedures) demonstrated a duplex closure rate of 89.4% at a

mean follow-up of 104 (±180) days with adverse thrombotic events in only two patients (0.5%).[28] Importantly, 79.8% of these procedures represented symptomatic failures of prior ipsilateral above-knee procedures, a scenario which is optimally suited to treatment with Varithena™. These and other series, also demonstrate that Varithena™, although not FDA approved for this indication, is a safe and effective treatment for symptomatic small saphenous vein reflux.

Tributary varicosities

Truncal reflux in the saphenous vein is often associated with visible tributary varicosities above or below the knee. Symptomatic tributary varicosities are usually managed with phlebectomy or foam sclerotherapy. The multi-societal guidelines for the management of varicose veins recommend ablation of refluxing venous trunks with concomitant phlebectomy or ultrasound guided foam sclerotherapy (GSV and SSV GRADE 1C; Accessory saphenous veins GRADE 2C).[4] Staged management of tributaries is suggested only in the presence of compelling anatomic or medical reasons. In comparison to catheter-based thermal and non-thermal ablation techniques, which address only truncal venous incompetence, PEM allows treatment of both truncal and symptomatic tributary reflux in a single setting using the same technology. It also allows varicosities in areas of skin damage below the knee to be safely treated. In a multicenter randomized trial, 117 patients were randomized to treatment of visible tributary varicosities with placebo, 0.5% PEM, or 1% PEM after undergoing concurrent thermal ablation.[17] As assessed by both patients and an expert clinician panel, a higher proportion of patients treated with PEM (pooled 0.5% and 1%) had a clinically meaningful improvement in appearance in comparison to placebo (physician assessed 83.5% vs 57.9% at week 8, p = .0004; patient assessed 72.2% vs 55.3% at week 8, p = .06). Although rates of SFJ reflux elimination were somewhat low in this study, they were higher in patients treated with thermal ablation + PEM (87.3%) than among those treated with thermal ablation + placebo (78.9%). In an observational study comparing PEM with EVLA, only 0.9% of patients initially treated with PEM (2 initial treatments in 17.1%) required follow-up treatment for recurrent symptoms in comparison to 18% of those treated with EVLA. Despite its utility in treating saphenous tributary varicosities, current coding structures require use of standard sclerotherapy codes for this indication, a limitation which is not financially feasible for many practices.

Venous leg ulcers

Venous leg ulcers have a prevalence of between 1.5 and three per 1000 people in the general population, increasing to about 20 per 1000 people over age 80.[29] Large randomized trials have demonstrated early venous ablation to improve ulcer healing (mean time to ulcer healing 56 days in comparison to 82 days for compression alone) and to reduce recurrence.[30] PEM has been similarly demonstrated to improve ulcer healing. In a multicenter, observational study of patients with particularly challenging ulcers, PEM ablation was associated with mean time to ulcer healing of 89 days (95% CI, 62.0 – 117.0 days) and a 13% ulcer recurrence rate 1 year after healing.[31] Although mean time to ulcer healing was longer than in the EVRA trial, the population in this study was particularly challenging with a higher BMI (36.3 ± 10.2), larger wounds (mean ulcer size 10.9 cm^2, circumferential in 26.3%), and a long ulcer duration (8.7 months). A second retrospective study comparing PEM and EVLA in 37 patients with venous ulcers demonstrated ulcer healing within 30 days in 69% and 5% of limbs respectively.[21] The improved efficacy with PEM may be related to both the ability to safely treat the below-knee GSV and the peri-ulcer venous plexus.[31]

Challenging anatomy and recurrent varicose veins

Catheter-based ablation techniques, whether thermal or non-thermal, generally require the truncal vein to be relatively straight with minimal tortuosity and to lack significant distortion, intraluminal synechia or segmental occlusion after an episode of superficial venous thrombosis or previously failed ablation. While such challenges can sometimes be managed using guidewires or multiple access points, as it is not primarily catheter-based, PEM is not subject to these limitations. The role of PEM in such challenging cases is well recognized.[32]

Recurrent varicose veins, or PREVAIT (*P*resence of *V*aricose *V*eins *A*fter *I*nterventional *T*reatment) require special consideration as many patterns of symptomatic recurrent reflux can be addressed only with foam sclerotherapy. Older surgical series suggested an incidence of recurrent varicose veins, which includes true recurrences, residual varices, and disease progression, of 20%–80% at 5 to 20 years after surgery, the incidence increasing over time.[33] Although modern ablation techniques have improved patient outcomes, they have not substantially changed the incidence of recurrence. The mode of recurrence is however different between HLS and thermal ablation. A meta-analysis of seven randomized clinical trials with at least 2 years follow-up demonstrated similar mid-term clinical recurrence rates of 21.4%, 20.6%, and 19.2% for RFA, EVLA, and HLS respectively (p = .98).[34] Neovascularization at the saphenofemoral junction was the most common cause of recurrence among limbs undergoing HLS while recanalization was most common (32%) after thermal ablation. Among limbs with recurrence, 57.9% of those treated with thermal ablation and 59.2% of limbs treated with HLS required treatment, with foam or liquid

sclerotherapy being the preferred form of treatment. For many causes of recurrence, such as neovascularization and recanalization with extensive intraluminal changes, foam sclerotherapy is the only option, with Varithena™, or PEM being the only foam sclerosant approved by the FDA.

Conclusions

Supported by robust data from two randomized clinical trials, Varithena™ was approved in 2013 as the only FDA approved foam sclerosant. Varithena™ has several favorable attributes setting it apart from physician-compounded foam. Its low nitrogen concentration and uniform small bubble size minimizes the risk of neurological complications, which are non-existent in most trials and case series, while its stability and cohesiveness are associated with greater endothelial disruption in both in vitro and ex vivo models.

Varithena™ was initially approved for the treatment of incompetent saphenous veins, accessory saphenous veins, and visible varicosities above and below the knee and was granted two category 1 CPT codes in 2018. These codes include 36465 and 36466 as follows,

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 – Multiple incompetent truncal veins (e.g., great saphenous vein, accessory saphenous vein) same leg.

These codes apply only to truncal veins, and when used outside of the truncal veins, regular sclerotherapy codes (35470, 36471) apply.

Since its approval, Varithena™ has been used to treat over 500,000 patients with clinical efficacy supported by an increasing number of peer reviewed studies as well as a systematic review and network meta-analysis. Consistent with the results of the pivotal trials, these studies suggest rates of symptomatic improvement and saphenous vein closure similar to those achieved with thermal ablation without the need for tumescent anesthesia. Perhaps more importantly, Varithena™ has clear advantages over other treatments in some specific circumstances. It allows treatment of the below knee GSV with minimal risk of saphenous nerve injury. It also allows treatment of challenging venous anatomy and recurrent patterns of reflux which cannot be optimally treated with catheter-based techniques. Finally, limited data does suggest some advantages to PEM over thermal techniques with respect to venous ulcer healing.

In conclusion, Varithena™ offers a safe and effective option to comprehensively treat a broad spectrum of patients with C2-C6 disease. The procedure is a straightforward, minimally invasive procedure, eliminating the need for potentially painful tumescent anesthesia and allowing treatment with as few as one or two access sites. Varithena allows treatment flexibility with clinical data supporting efficacy in challenging anatomy and a wide variety of diameters up to 25.9 mm above and below the knee. Foam sclerotherapy is often the best or only option for treating some patterns of reflux (the below-knee GSV, recurrent reflux in a recanalized saphenous veins) and Varithena™ remains the only FDA approved foam sclerosant. There is also evidence of superior efficacy in comparison to PCF.[8] Based on the published evidence, the American Vein and Lymphatic Society supports Varithena as a safe, effective, and clinically meaningful option for the treatment of superficial venous disease. Most major health insurance plans in the United States, including Medicare, cover Varithena for FDA-approved indications, although it is still categorized as a secondary treatment option or "investigational" therapy by a few outliers. Such a designation is clearly inappropriate given the volume of clinical data demonstrating the safety and efficacy of Varithena™ in a variety of clinical settings. Based upon clinical experience and the published data, the AVLS also supports efforts to expand the approved indications for Varithena beyond the great saphenous, accessory saphenous, and associated tributary varicosities. Such indications would include the treatment of neovascular tributaries contributing to recurrent symptoms after previous intervention and treatment of the small saphenous vein.

Varithena™ is a registered trademark of Boston Scientific Corporation

Declaration of conflicting interests

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Ethical statement

Ethical approval

This article includes no original research on human or animal subjects, reporting only previously published peer-reviewed data. Our institution does not require ethical approval for review articles.

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