

**Position Statement
Healthcare Policy Committee
Cyanoacrylate Venous Closure**

REVISED: February 28, 2019

Introduction

Historically, treatment options for patients with venous insufficiency and varicose veins primarily consisted of high ligation and stripping of the great saphenous vein (GSV) in association with phlebectomy and sclerosant injection of individual varicosities. During the past 18 years, such painful interventions, which required general anesthesia along with several days in the hospital and weeks of recuperation, have been supplanted by outpatient office-based endovascular ablation techniques with conscious sedation and/or local anesthesia and an almost immediate return to normal activities of daily living. Such endovascular treatment of venous disease has been primarily performed with thermally-based radiofrequency or laser ablation that require percutaneous, perivenous tumescent anesthesia. They are superior to high ligation and stripping and are recommended by published multi-society guidelines for the treatment of the incompetent superficial axial incompetent veins (GSV, SS, AASV etc.) [Gloviczki P et al. ***The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum.*** *J Vasc Surg.* 2011;53(5 suppl):2S-48S] With these approaches, patients achieve excellent vein occlusion rates and more importantly improved quality of life for years after intervention.

Newer approaches have significantly improved thermal ablation methods by achieving similar clinical outcomes without thermal energy and thus obviate the need for tumescent anesthesia. Elimination of tumescent anesthesia results in less recovery time, no risk of nerve injury and minimal skin damage, and ability to treat distally below the knee due to the lack of heat, which may be particularly important in the setting in venous leg ulcers. The opportunity for physicians to have a choice of treatment options in order to choose the one that is optimal for an individual patient will result in the best outcomes in the treatment of venous insufficiency and varicose veins.

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Cyanoacrylate Closure (CAC): VenaSeal™ Closure System The VenaSeal™ Closure System is the only FDA approved non-tumescent, non-thermal, *non-sclerosant* treatment for patients suffering with symptomatic venous reflux disease in the United States. The VenaSeal™ Closure System, a n-butyl-2-cyanoacrylate (n-BCA) based formulation polymerizes in the vessel upon contact with body fluids or tissue. This acute process halts blood flow through the diseased vein until the implanted adhesive becomes encapsulated and fibrosed to establish a durable, chronic occlusion of the treated vein. It is administered while using high resolution ultrasound imaging for precise placement of the adhesive.

The procedure has four core phases: catheter insertion, adhesive administered, compression and occlusion. No post-procedure compression stockings are required*. The procedure is typically performed in a physician's office setting but can also be provided in a hospital outpatient setting. It is another first-line option for insufficient truncal veins, that often allows individual saphenous veins to be treated in a single visit. With published outcomes of the treatment of veins up to 20mm¹, VenaSeal™ Closure System affords improved patient experience and safety with the elimination of thermal energy and tumescent anesthesia. Multiple studies have included QOL measures demonstrating significant symptomatic improvement

On February 20, 2015, the U.S. Food and Drug Administration (FDA) granted premarket approval (PMA) of the VenaSeal™ Closure System (VSCS) as "an implantable device indicated for the permanent closure of lower extremity superficial truncal veins, such as the great saphenous vein (GSV), through endovascular embolization with coaptation. The VenaSeal™ Closure System is intended for use in adults with clinically symptomatic venous reflux as diagnosed by duplex ultrasound (DUS)." The FDA mandated physician training is a rigorous process to ensure the VenaSeal™ Closure System is delivered effectively and consistent outcomes are achieved.

As of January, 2019, there have been over 90,000 successful VenaSeal™ Closure System procedures performed worldwide in patients suffering from chronic venous insufficiency ranging from CEAP 2 through CEAP 6.

¹ Gibson K and 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; 25: 149–156.

CPT codes describing cyanoacrylate for the treatment of incompetent veins went into effect on January 1, 2018:

- 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)

Conclusion

The current published evidence, and FDA approval as an implantable device, support VenaSeal™ Closure System as a safe, effective and clinically meaningful option for the treatment of superficial venous disease when it is deemed to be medically necessary. The American Vein and Lymphatic Society, on behalf of our members and their patients, request that carriers cover VenaSeal™ Closure System for all FDA-approved indications with reimbursement commensurate with CMS valuation, or by contract with private payers. Attached are the clinical data and references to substantiate our recommendations.

Select Bibliography:

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Number of Peer Reviewed Articles:

Currently, there are over 37 peer reviewed articles, review articles, case reports, and editorials, including the pivotal RCT 36 months VeClose, (60 months VeClose results to be presented at Charing Cross April 2019), that have been published regarding VenaSeal and its safety and/or efficacy.

Year of FDA Approval:

FDA PMA approval was granted on February 20, 2015

Date of First Human Use:

First in Man study completed enrollment in December 2010 and July 2011 respectively. There were also 2 pre-clinical studies:

- Min RJ, Almeida JI, et al Novel vein closure procedure using a proprietary cyanoacrylate adhesive: 30-day swine model results, *Phlebology* 2012:1-6
- Almeida JI, Min RJ, Raabe R, et al. Cyanoacrylate adhesive for the closure of truncal veins: 60-day swine model results. *Vasc Endovasc Surg* 2011; 45: 631-635.

Number of Patients Treated:

At the current time, there have been more than 90,000 patients treated world-wide with VenaSeal™ Closure System

Summary of Clinical Evidence:

The clinical evidence supporting the safety and effectiveness of the VenaSeal™ Closure System is derived from a combination of four clinical studies. The four main studies are:

- Feasibility Study
- eScope
- VeClose
- WAVES

The primary clinical study (VeClose) was a controlled, randomized, prospective, multicenter, pivotal study in which patients with venous reflux in the great saphenous vein (GSV) were treated with either the VenaSeal™ system or radiofrequency ablation (RFA) therapy. The goal of the study was to show statistical noninferiority of cyanoacrylate adhesive embolization (CAE) efficacy compared with radiofrequency ablation (RFA).² Patients were treated between March 11, 2013 and September 11, 2013, with 242 patients (including 20 roll-in patients) enrolled at 10 investigational sites in the United States. Following treatment, subjects were followed at 3 days, and 1, 3, 6, 12, 24, and 36 months. No adjunctive treatments were permitted until after the 3-month follow-up visit to allow for evaluation of success of the truncal closure of the VenaSeal™ Closure system.

The table below for the VeClose study shows complete closure rates of targeted GSV at specified timeframes, including results from recently published 24-month and 36-month data which show the effective and durable closure rate of 95.3% and 94.4% for cyanoacrylate compared to 94% and 91.9% for RFA, respectively.⁴

Timepoint	VenaSeal (N=108)	RFA (N=114)	Roll-In (N=20)
Day 3	100% (108/108)	99.1% (113/114)	100.0% (20/20)
Month 1	100% (105/105)	86.4% (95/110)	100.0% (20/20)
Month 3	99% (103/104)	95.4% (103/108)	100.0% (19/19)
Month 6	99% (100/101)	94.3% (99/105)	100.0% (17/17)
Month 12	96.8% (92/95)	96.8% (91/94)	100.0% (17/17)
Month 24	95.3% (82/86)	94.0% (79/84)	87.5% (14/16)
Month 36	94.4% (68/72)	91.9% (68/74)	94.1% (16/17)

Through 36-month follow-up, the rate of adverse event (AE) occurrence was similar among the two treatment groups. During months 24–36, there were only two AEs reported in the Cyanoacrylate Closure (CAC) group and no device-related or procedure-related AEs in the RFA group. One case of late onset phlebitis was CAC procedure-related while the case of scar was directly related to the both CAC procedure/device. Although not statistically significant, phlebitis or a general inflammatory response along the treated vein was more common in the CAC group. This was treated solely with non-steroidal anti-inflammatory drugs in both groups and was self-limiting. No pulmonary emboli or deep venous thrombi occurred in either group.³

There are over 37 published studies and reports on the use of the VenaSeal™ Closure system which not only include closure rates which are non-inferior to RFA but show improved QOL measures using a variety of different tools.

² Morrison N, Gibson, K et al, Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose), J Vasc Surg 2015;61:985-94.)

³ Morrison N, Kolluri R, Vasquez M, Madsen M, Jones A, Gibson K. 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: 1-11

Evidence Conclusion:

VenaSeal™ Closure System, as a non-thermal, NTNS treatment modality, provides a treatment option that demonstrates a high level of safety and efficacy, and offers the following important benefits: elimination of the risk/concern of lidocaine toxicity; allergy with tumescent anesthesia and thermal nerve injury; absence of venous thrombosis; no requirement for post-procedure compression stockings*; and greatly improved patient comfort due to elimination of multiple needle sticks, associated bruising, and reduced recovery/recuperation time. The 36-month occlusion rate (94.4%) of the target GSV with CAC in the VeClose trial is similar to the rate reported in a three-year follow-up, first-human-use CAC study (94.7%).⁴ Further, VeClose data through 36 months reports similar GSV closure rates with both CAC and RFA, further confirming the durability and non-inferiority of CAC compared to RFA. In addition, VCSS and QoL significantly improved from baseline to six months and were maintained at 36 months in both treatment groups as noted in the VeClose study.

⁴ Almeida JJ, Javier JJ, Mackay EG, et al. Thirty-sixth month follow-up of first-in-human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. *J Vasc Surg Venous Lymphat Disord* 2017; 5: 658–666.

*Some patients may benefit from the use of compression stockings post-procedure