VARICOSE VEINS

CHI Formulary Development Project

مجلس الضمان الصحي
Council of Health Insurance

September 2023

Contents

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

List of Tables

List of Figures

Abbreviations

AAGSV	Anterior Accessory Great Saphenous Vein
ARTE	Ablation Related Thrombus Extension
ASVAL	Ambulatory Selective Variceal Ablation Under Local Anesthesia
AVF	American Venous Forum
AVLS	American Vein and Lymphatic Society
CAC	Cyanoacrylate Adhesive Closure
CDFS	Catheter Directed Foam Sclerotherapy
CEAP	Comprehensive Classification System for Chronic Venous Disorders
CHI	Council of Health Insurance
CHIVA	Cure Conservatrice et Hemodynamique de l'Insuffisance Veineuse en Ambulatoire
CTV	Computed Tomography Venography
CVD	Chronic Venous Disease
DVS	Deep Venous System
DVT	Deep Venous Thrombosis
EBP	Essential Benefits Package
EHIT	Endovenous Heat-Induced Thrombosis
EMA	European Medicines Agency
EVLA	Endovenous Laser Ablation
FDA	Food and Drug Administration
GP	General Practitioner
GSV	Great Saphenous Vein
HLS	High Ligation and Stripping
IDF	CHI Drug Formulary
IPV	Incompetent Perforating Veins
KSA	Kingdom of Saudi Arabia

LEED	Laser Energy Density
LMWH	Low Molecular Weight Heparin
MOCA	Mechanochemical Ablation
MPFF	Micronized Purified Flavonoid Fraction
MRV	Magnetic Resonance Venography
NSAID	Non-Steroidal Anti-Inflammatory Drug
OCP	Oral Contraceptive Pills
PAGSV	Posterior Accessory Great Saphenous Veins
PCF	Physician-Compound Foam
PEM	Polidocanol Endovenous Microfoam
PPG	Photoplethysmography
PTS	Post-Thrombotic Syndrome
RFA	Radiofrequency Ablation
SFDA	Saudi Food and Drug Authority
SPJ	Saphenopopliteal Junction
SSV	Small Saphenous Veins
SVS	Society for Vascular Surgery
SVT	Superficial Vein Thrombosis
UGFS	Ultrasound-Guided Foam Sclerotherapy
UGS	Ultrasound-Guided Sclerotherapy
VCSS	Venous Clinical Severity Score
VKA	Vitamin K Antagonist
VOP	Venous Occlusion Plethysmography
VTE	Venous Thromboembolism
VV	Varicose Veins

Executive Summary

Varicose veins (VV) are twisted, dilated veins most commonly located on the lower extremities. VV are **subcutaneous** veins dilated to at least 3 mm in diameter when measured with the patient in an upright position. They are part of a continuum of **chronic venous disorders** ranging from fine telangiectasias, also called spider veins, (less than 1 mm) and reticular veins (1 to 3 mm) to chronic venous insufficiency, which may include edema, hyperpigmentation, and venous ulcers. Chronic venous disease is most commonly described using the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification system (table 12 below)[1].

Varicose veins are common on the lower extremities, with widely varying estimates of prevalence. A recent study found that telangiectasias occur in 43% of men and 55% of women, and varicose veins occur in 16% of men and 29% of women. In a population with a mean age of **60 years**, the prevalence of CEAP classification C0 to C6 is 29%, 29%, 23%, 10%, 9%, 1.5%, and 0.5%, respectively[2].

Venous disease resulting in valvular reflux appears to be the underlying **cause** of varicose veins. The exact **pathophysiology** is debated, but it involves a genetic predisposition, incompetent valves, weakened vascular walls, and increased intravenous pressure. In most cases, the valvular dysfunction is presumed to be caused by a loss of elasticity in the vein wall, with failure of the valve leaflets to fit together. Rather than blood flowing from distal to proximal and superficial to deep, failed or incompetent valves allow blood to flow in the reverse direction. With increased pressure on the affected venous system, the larger veins may become elongated and tortuous. Shear stress on venous endothelial cells due to reversed or turbulent blood flow and inflammation are also important etiologic factors for venous disease. Varicose veins in the legs may involve the **main axial superficial veins** (the great saphenous vein and the small saphenous vein or their superficial tributaries).

Risk factors include:

- Family history of venous disease
- Female sex
- Older age
- Chronically increased intra-abdominal pressure due to obesity
- Pregnancy
- Chronic constipation
- Tumor
- Prolonged standing: according to a study done in Al-Ahsa, Saudi Arabia, teachers have a significant chance of developing the condition since their working style contributes to its progression[3]

- Deep venous thrombosis causing damage to valves and secondary revascularization
- Arteriovenous shunting

A **study done in KSA** showed a significant relationship between the presence of varicose veins and age group, gender, alcohol consumption, long duration of sitting and standing hours, family history of varicosities, history of leg surgery, frequent constipation, pregnancy more than once, and hormonal therapies including oral contraceptive pills (OCP)[4].

The **clinical presentation** of varicose veins varies, and some patients may be asymptomatic. Localized symptoms may be unilateral or bilateral and include pain, burning, itching, and tingling at the site of the varicose veins. Generalized symptoms consist of aching, heaviness, cramping, throbbing, restlessness, and swelling in the legs. Symptoms are often worse at the end of the day, especially after prolonged standing, and usually resolve when patients sit and elevate their legs. Patients are more likely to have symptoms and increasing severity of symptoms with increasing CEAP clinical class (C0 to C6).

Although varicose veins may cause varying degrees of discomfort or cosmetic concern, they are rarely associated with significant complications. **Signs of a more serious underlying vascular insufficiency** may include changes in skin pigmentation, eczema, infection, superficial thrombophlebitis, venous ulceration, loss of subcutaneous tissue, and lipodermatosclerosis[5].

Evaluation of patient risk factors, symptoms, and typical physical examination findings helps determine a diagnosis. When venous disease is severe or interventional therapy is being considered, **venous duplex ultrasonography** is the modality of choice. The **prevalence** of varicose veins varies geographically. Worldwide, the incidence of varicose veins varies between 10% and 60%. This incidence is higher in the Asian region as compared to up to 30% in the Western world. Studies have shown the prevalence to be as high as **62% in Saudi Arabia**, with increasing annual incidence of about 5% in females and 2% in males[6].

This report compiles all clinical and economic evidence related to Varicose Veins according to the relevant sources. The ultimate objective of issuing VV guidelines by the Council of Health Insurance (CHI) is to update the IDF (CHI Drug Formulary) with the **best available clinical and economic evidence related to drug therapies, ensuring timely and safe access to VV patients in Saudi Arabia**. The main focus of the review was on North American, European guidelines and international guidelines (mainly Australian) issued within the last five years.

While some guidelines are more general and describe venous insufficiency management, some other are mainly related to varicose veins with specific therapeutic management. To elaborate **North American guidelines** included the

Society for Vascular Surgery (SVS), American Venous Forum (AVF), and American Vein and Lymphatic Society (AVFLS) clinical practice guidelines in two parts. Part I was published in 2022 and focuses on duplex scanning and the treatment of superficial truncal reflux. Part 2 was published in 2023 and it includes details concerning the management of varicose veins: conservative therapy, pharmacotherapy; interventional therapy and the management of varicose veins complications. **European guidelines** included NICE guidelines; ESVS recommendations and S2K guidelines. NICE guidelines included the assessment, interventional and non-interventional treatment and the management of varicose veins during pregnancy. ESVS recommendations has focused on the scoring systems, compression therapy, pharmacotherapy and interventional therapy. S2K guidelines drew focus on the classification, diagnosis, treatment and management during pregnancy. **International guideline** included the treatment of VV.

Main recommendations issued by different **Health Technology Assessment** (HTA) bodies on the use of the current medications in VV were reviewed and summarized. These include the National Institute for Health and Care Excellence (NICE), the Canadian Agency for Drugs and Technologies in Health, Haute Autorité de Santé (HAS), the Institute for Quality and Efficiency in Healthcare (IQWIG), and the Pharmaceutical Benefits Advisory Committee (PBAC). Section 3 lists the key recommendations synthesis for VV treatment

Treatment options for varicose veins include **conservative management**, **pharmacotherapy**, **external laser treatment**, **injection sclerotherapy**, **endovenous interventions**, and **surgery**. The indications for treatment are largely based on patient preference.

The **goals** of varicose veins treatment are to **reduce symptoms** and **prevent complications**. For some, the goal may be **improved appearance**. Home treatment is typically the first approach[7].

Choice of treatment is also affected by symptoms, cost, potential for iatrogenic complications, available medical resources, insurance reimbursement, and physician training, as well as the presence or absence of deep venous insufficiency and the characteristics of the affected veins. *The CHI essential benefits package (EBP) covers the management of symptoms and complications that are **not** related to cosmetic appearance improvement.*

Vascular surgical intervention for venous insufficiency may be indicated in patients with aching pain and leg fatigue, ankle edema, chronic venous insufficiency, early hyperpigmentation, external bleeding, progressive or painful ulcer, or superficial thrombophlebitis.

Studies of treatments for varicose veins are **limited** by small numbers of study participants, short follow-up, and inconsistent end points (e.g., resolution of

symptoms, ultrasonography measurements, appearance as judged by the patient or physician).

The number of drugs that are SFDA approved for the management of VV is still **limited**. KSA has access to four approved treatments only (aescin, diosmin (+ hesperidin), calcium dobesilate; pentoxifylline). Section 2 provides a full description of each with final statements on the placement of therapy. All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) reflecting specific drug class role in the management ofVV.

The strongest recommendations include:

- For chronic venous diseases, we advocate using the 2020 updated **CEAP** categorization system in clinical research and practice.
- Duplex ultrasonography (**DUS**) should be used for accurate and consistent diagnosis of reflux in the superficial veins; standardized protocols exist for sonographers, as well as standardized definitions of abnormal reflux.
- **Intervention** is the best treatment for patients with symptomatic varicose veins and reflux and is preferred to prolonged long-term use of **compression** stockings, which does not relieve the underlying cause of venous reflux and insufficiency.
- **Compression therapy** is suggested immediately after treatment of superficial veins with sclerotherapy to improve outcomes of sclerotherapy.
- Treatment of systematic axial vein reflux should be treated primarily with **endoluminal thermal or nonthermal ablation** techniques rather than with surgical vein stripping.
- Tributary varicosities can be treated either with direct **phlebectomy or with ultrasound-guided foam sclerotherapy.**
- **Pharmacotherapy** is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention.
- **Exercise** should be taken into consideration for people with symptomatic chronic venous illness in order to lessen venous symptoms (Class of recommendation: IIa; Level of evidence: B)
- **Interventional therapy** is recommended for individuals with superficial venous incompetence who present with symptomatic varicose veins.

Major recommendations for suggested drug therapies are summarized in the table below:

For SFDA Registered Drugs:

Table 1. Major Recommendations for SFDA Registered Drugs Used for the Management of Varicose Veins

Medication	Indication	Level of Evidence/ Recommendation	HTA Recommendations
Aescin	Is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention	Class of recommendation: IIa Level of evidence: A	The HTA bodies did not issue any recommendation on the cost effectiveness of Aescin
Diosmin	Is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention	Class of recommendation: IIa Level of evidence: A	The HTA bodies did not issue any recommendation on the cost effectiveness of Diosmin

Hesperidin	Is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention	Class of recommendation: IIa Level of evidence: A	The HTA bodies did not issue any recommendation on the cost effectiveness of Hesperidin
Calcium Dobesilate	Is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention	Class of recommendation: IIa Level of evidence: A	The HTA bodies did not issue any recommendation on the cost effectiveness of Calcium Dobesilate
Pentoxifylline	Is recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are	Class of recommendation: IIa Level of evidence: A	HAS: It is possible to use pentoxifylline in addition to compression to treat venous ulcers.

	waiting for intervention, or have symptoms after intervention		

Table 2. Management Options for Varicose Veins

Treatment Options	Comments
Conservative Measures	
Compression (e.g., bandages, support stockings, intermittent pneumatic compression devices)	Support stockings can provide relief from discomfort.
Elevation of the affected leg	Elevation may improve symptoms in some patients.
Lifestyle modifications	Examples include avoidance of prolonged standing, exercise, loosening of restrictive clothing, modification of cardiovascular risk factors, and reduction of peripheral edema
Weight loss	Weight loss may improve symptoms in patients who are obese.
Pharmacotherapy	For the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention
Endovenous or Interventional Therapy	
Endovenous obliteration	Randomized controlled trials comparing clinical effectiveness and cost-effectiveness are lacking.
External laser therapy	
Sclerotherapy	
Surgery	
Ligation	Historically, surgery has been the most widely recommended treatment option.
Phlebectomy	
Stripping	

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

1.1 North American Guidelines

Multiple organizations have published guidelines for the management of Varicose Veins, most notably the Society for Vascular Surgery (SVS), American Venous Forum (AVF), and American Vein and Lymphatic Society (AVLS) in two parts (Part I and Part II). Recommendations of those guidelines are detailed in the following section:

1.1.1 SVS/AVF/AVLS Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities – Part I (2022)

Part I of the guidelines published jointly by SVS, AVF, and AVLS mainly tackled duplex scanning and the treatment of superficial truncal reflux[8]. The main recommendations are summarized below.

Diagnostic evaluation of vein incompetence

- **Duplex ultrasound** scanning is recommended as the diagnostic **test of choice** for individuals with chronic venous illness of the lower extremities to evaluate for venous reflux (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- A **minimum value of > 500 ms** of reversed flow in the superficial truncal veins, as well as the tibial, deep femoral, and perforating veins, is characterized as reflux. A minimum value of **more than one second** of reversed flow indicates reflux in the common femoral, femoral, and popliteal veins (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- In patients with varicose veins, perforating veins classified as "**pathologic**" (CEAP [Clinical Class, Etiology, Anatomy, Pathology] clinical class C2 include those with an outward flow duration of more than 500 ms and a diameter of more than 3.5 mm on duplex ultrasonography) have a diameter more than 500 ms (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate)).
- A credentialed **ultrasonographer** should evaluate reflux using duplex ultrasonography at an Intersocietal Accreditation Commission or American College of Radiology-accredited vascular laboratory, with the patient standing whenever possible. If the patient is unable to stand, a sitting or reverse Trendelenburg position can be used (Level of recommendation: ungraded good practice statement)

- When evaluating reflux with duplex ultrasound we recommend using a **Valsalva maneuver or distal augmentation** to assess the common femoral vein and saphenofemoral junction and distal augmentation with either manual compression or cuff deflation (Level of recommendation: ungraded good practice statement)
- Superficial reflux must be traced back to its source, which could be the saphenous junctions, truncal or perforating veins, or varicose veins of pelvic origin. A physician trained in venous duplex ultrasonography interpretation should interpret the study (Level of recommendation: ungraded good practice statement)
- A complete duplex ultrasound scanning examination for venous reflux in the lower extremities should include **transverse grayscale images** of the common femoral, proximal, mid, and distal femoral and popliteal veins, saphenofemoral junction, and great and small saphenous veins without and with transducer compression (Level of recommendation: ungraded good practice statement)
- A comprehensive duplex ultrasound scanning evaluation for venous reflux in the lower extremities should include **caliper measurements of the spectral Doppler waveform**. Any reflux at baseline and in response to a Valsalva maneuver or distal augmentation should be documented (Level of recommendation: ungraded good practice statement)
- A thorough duplex ultrasound scanning evaluation for venous reflux in the lower extremities should include **diameter measurements** in patients with the leg in the dependent position. Images of both normal and abnormal findings should be documented in the records of the patient (Level of recommendation: ungraded good practice statement)
- For chronic venous diseases, using the **2020 updated CEAP categorization system** (table 3) in clinical research and practice is recommended (Level of recommendation: ungraded good practice statement)

Table 3. Updated Clinical, Etiology, Anatomy and Pathology (CEAP) Classification of Chronic Venous Disorders (Adapted from SVS/AVF/AVLS 2022 Guidelines)

Class	Description
Clinical	
C0	No visible or palpable signs of venous disease
C1	Telangiectasis or reticular veins
C2	Varicose veins

C2r	Recurrent varicose veins
C3	Edema
C4	Changes in skin and subcutaneous tissue due to chronic venous insufficiency
C4a	Pigmentation or eczema
C4b	Lipodermatosclerosis or atrophie blanche
C4c	Corona phlebectatica
C5	Healed venous ulcer
C6	Active venous ulcer
C6r	Recurrent active venous ulcer
Etiology	
Ec	Congenital
Ep	Primary
Es	Secondary (post-thrombotic)
En	No venous etiology identified
Anatomy	
As	Superficial veins
Ap	Perforator veins
Ad	Deep veins
An	No venous location identified
Pathophysiology	
Pr	Reflux
Po	Obstruction
Pr,o	Reflux and obstruction
Pn	No venous pathophysiology identifiable

High ligation and surgical stripping vs endovenous ablation

- **Superficial venous intervention** is preferred over long-term compression stockings for patients with symptomatic varicose veins with axial reflux in the great or small saphenous veins (**GSV or SSV**) who are suitable for intervention (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))

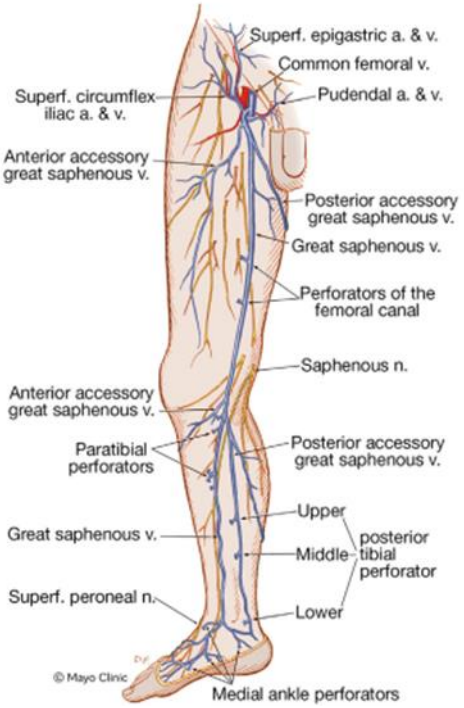


Figure 1. *Anatomy of Great Saphenous Vein (GSV) and its Tributaries (Retrieved from SVS/AVF/AVLS 2022 Guidelines)*

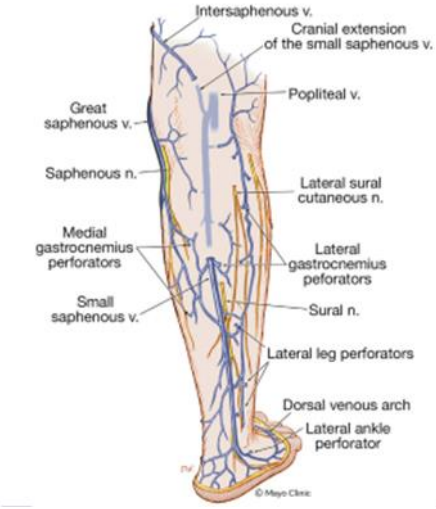


Figure 2. *Anatomy of Small Saphenous Vein (SSV) and its Tributaries (Retrieved from SVS/AVF/AVLS 2022 Guidelines)*

- We recommend **superficial venous intervention** over compression stockings for patients with symptomatic varicose veins with axial reflux in the anterior or posterior accessory great saphenous veins (**AAGSV or PAGSV**) who are suitable for intervention (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))

- **Compression therapy** is recommended for patients with symptomatic varicose veins and axial reflux in the superficial truncal veins as primary treatment if the patient's ambulatory status and underlying medical conditions warrant it, or if the patient prefers conservative treatment for either a trial period or definitive management (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- **Endovenous ablation** is recommended over high ligation and stripping of the great saphenous vein for patients with symptomatic varicose veins and axial reflux in the great saphenous vein who are candidates for intervention due to less postprocedure pain and morbidity and an earlier return to regular activity (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- **Endovenous ablation** is recommended over ligation and stripping of the small saphenous vein for patients with symptomatic varicose veins and axial reflux in the small saphenous vein who are candidates for intervention because it results in less postprocedure pain and morbidity and an earlier return to regular activity (Level of recommendation: grade 1 (strong), quality of evidence: C (low to very low))
- **Endovenous ablation with additional phlebectomy**, if needed are recommended over ligation and stripping of the accessory great saphenous vein for patients with symptomatic varicose veins and axial reflux in the anterior or posterior accessory great saphenous vein who are candidates for intervention due to less postprocedure pain and morbidity and an earlier return to regular activity (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- If endovenous ablation technology or expertise is unavailable, or if the venous anatomy precludes endovenous treatment, **ligation and stripping** of the saphenous vein is recommended for patients with symptomatic varicose veins and axial reflux in the great or small saphenous vein (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- For patients with symptomatic varicose veins and axial reflux in the anterior or posterior accessory great saphenous vein, **ligation and stripping of the accessory great saphenous vein, with additional phlebectomy** if necessary, should be performed if endovenous ablations are not available or if the venous anatomy precludes endovenous treatment (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- **Endovenous laser ablation** (EVLA), **radiofrequency ablation** (RFA), or **high ligation and stripping** are recommended and preferred over physician-compounded ultrasound-guided foam sclerotherapy for patients with symptomatic varicose veins and axial reflux in the **great saphenous** vein who

place a high priority on long-term treatment outcomes (quality of life and recurrence) (Level of recommendation: grade 2 (weak) quality of evidence: B (moderate))

- Laser ablation, RFA, or ligation and stripping from the knee to the upper or mid-calf are recommended over physician-compounded ultrasound-guided foam sclerotherapy (UGS) for patients with symptomatic varicose veins and axial reflux in the **small saphenous** vein who place a high priority on long-term treatment outcomes (quality of life and recurrence) (Level of recommendation: grade 2 (weak) quality of evidence: C (low to very low))
- Endovenous laser ablation, radiofrequency ablation or high ligation and stripping, with additional phlebectomy if necessary, are recommended over physician-compounded ultrasound-guided foam sclerotherapy for patients with symptomatic varicose veins and axial reflux in the **anterior or posterior accessory** great saphenous veins who place a high priority on long-term treatment outcomes (quality of life and recurrence) (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))

Thermal ablation vs nonthermal ablation of saphenous veins

- For patients with symptomatic axial reflux of the great saphenous vein, **both thermal and nonthermal ablation** from the groin to below the knee, depending on the treating physician's available skill and the patient's preference are recommended (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- For patients with symptomatic axial reflux of the small saphenous vein, **both thermal and nonthermal ablation** from the knee to the upper or mid-calf, depending on the treating physician's available skill and the patient's preference are recommended (Level of recommendation: grade 1 (strong), quality of evidence: C (low to very low))
- We suggest **either thermal or nonthermal ablation, with additional phlebectomy**, if necessary, for patients with symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein, depending on the treating physician's expertise and the patient's preferences (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))

Incompetent perforating veins ablation in patients with CEAP class C2 varicose veins

- Treating incompetent perforating veins (IPV) **concurrently** with initial superficial truncal vein ablation in patients with varicose veins (CEAP class C2) who have considerable, symptomatic axial reflux of the great or small

saphenous vein **is not recommended** (Level of recommendation: grade 1 (strong), quality of evidence: C (low to very low))

- Treating IPV concurrently with initial superficial truncal vein ablation in patients with varicose veins (CEAP class C2) who have considerable, symptomatic axial reflux of the anterior accessory or posterior accessory great saphenous vein **is not suggested** (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- Treating perforating vein incompetence (if it is the cause of the symptomatic varicose tributaries) in individuals with varicose veins (CEAP class C2) and persistent or recurring symptoms following **prior full ablation** of incompetent superficial truncal veins is recommended (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))

Ablation of the refluxing symptomatic superficial venous trunk and concomitant treatment of varicose tributaries

- **Ablation** of the refluxing venous trunk and **concurrent phlebectomy** or **ultrasound-guided foam sclerotherapy** of the varicosities with doctor-prepared foam or commercial polidocanol endovenous microfoam are recommended for patients who have symptoms of reflux in the great or small saphenous vein and associated varicosities (Level of recommendation: grade 1 (strong); quality of evidence: C (low to very low))
- Ablation of the refluxing venous trunk and **concurrent** phlebectomy or ultrasound-guided foam sclerotherapy of the varicosities with doctor-prepared foam or commercial polidocanol endovenous microfoam are **suggested** for patients with symptoms of reflux in the anterior accessory or posterior accessory great saphenous vein (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- Ablation of the refluxing venous trunk and **staged phlebectomy** or ultrasound-guided foam sclerotherapy of the varicosities are suggested only if anatomical or medical reasons exist in individuals with symptoms of reflux in the great or small saphenous vein and in the anterior accessory great saphenous vein or posterior accessory great saphenous vein (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- Patients should be monitored for **three months** after initial ablation in those with symptomatic reflux in the major superficial venous trunks and associated varicosities in order to determine whether staged phlebectomy or ultrasound-guided sclerotherapy is necessary for persistent or recurrent symptoms. Patients who take part in clinical trials and those with recurrent symptoms

should have a longer follow-up (Level of recommendation: ungraded good clinical practice)

1.1.2 SVS/AVF/AVLS Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities – Part II (2023)

Part II focuses on evidence supporting the prevention and management of varicose vein with compression, on the pharmacological treatment and nutritional supplements, on the evaluation and treatment of varicose tributaries, on superficial venous aneurysms, and on the management of complications of varicose veins and their treatment[9]. The main recommendations are detailed below.

Classification and grading of clinical severity of chronic venous disorders

- For the grading of clinical severity and the evaluation of post-treatment results in patients with chronic venous diseases, we advise the use of the updated **Venous Clinical Severity Score** (VCSS) detailed in table 4 (Level of recommendation: ungraded good practice statement)

Table 4. Revised Venous Clinical Severity Score (VCSS) (Retrieved from the SVS/AVF/AVLS 2023 Guidelines)

Pain or other discomfort (i.e., aching, heaviness, fatigue, soreness, burning) Presumes venous origin	**None:** 0	**Mild:** 1 Occasional pain or other discomfort (i.e., not restricting regular daily activity)	**Moderate:** 2 Daily pain or other discomfort (i.e., interfering with but not preventing regular daily activities)	**Severe:** 3 Daily pain or discomfort (i.e., limits most regular daily activities)
Varicose veins "Varicose" veins must be ≥3 mm in diameter to qualify	**None:** 0	**Mild:** 1 Few: scattered (i.e., isolated branch varicosities or clusters) Also includes corona phlebectatica (ankle flare)	**Moderate:** 2 Confined to calf or thigh	**Severe:** 3 Involves calf and thigh
Venous edema Presumes venous origin	**None:** 0	**Mild:** 1 Limited to foot and ankle area	**Moderate:** 2 Extends above ankle but below knee	**Severe:** 3 Extends to knee and above
Skin pigmentation Presumes venous origin Does not include focal pigmentation over varicose veins or pigmentation due to other chronic diseases (i.e., vasculitis purpura)	**None:** 0 None or focal	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Inflammation More than just recent pigmentation (i.e., erythema, cellulitis, venous eczema, dermatitis)	**None:** 0	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Induration Presumes venous origin of secondary skin and subcutaneous changes (i.e., chronic edema with fibrosis, hypodermitis) Includes white atrophy and lipodermatosclerosis	**None:** 0	**Mild:** 1 Limited to perimalleolar area	**Moderate:** 2 Diffuse over lower third of calf	**Severe:** 3 Wider distribution above lower third of calf
Active ulcer number	0	1	2	≥3
Active ulcer duration (longest active)	N/A	<3 months	>3 months but <1 year	Not healed for >1 year
Active ulcer size (largest active)	N/A	Diameter <2 cm	Diameter 2–6 cm	Diameter >6 cm
Use of compression therapy	0 Not used	1 Intermittent use of stockings	2 Wears stockings most days	3 Full compliance: stockings

Duplex ultrasound scanning (DUS)

- It is not recommended to routinely undertake **DUS** assessment of the lower extremity veins in asymptomatic individuals with **telangiectasias or reticular veins** (CEAP Class C1) since doing so could lead to unneeded saphenous vein ablation treatments (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- Saphenous ablation for C1 disease without bleeding is rarely required. In symptomatic CEAP Class C1 patients with bleeding or with severe symptoms of pain or burning due to moderate to severe telangiectasias or reticular veins, DUS **evaluation** may be performed to rule out associated venous

incompetence (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))

- Deep venous system evaluations for infrainguinal blockage or valvular incompetence should be **performed** routinely in symptomatic varicose vein patients (CEAP Class C2 patients) (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- In **symptomatic** patients with varicose veins (CEAP Class C2) if suprapubic or abdominal wall varicosities are present, as well as in patients who have symptoms of proximal obstruction, such as thigh and leg fullness, heaviness, swelling, and venous claudication, evaluation for iliofemoral venous obstruction with DUS or with other imaging studies should be carried out (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- A **DUS** or other imaging study is necessary to check for iliofemoral blockage in CEAP Classes 3-6 (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- If a patient has medial thigh or vulvar varicosities without any indications of pelvic venous illness, examination of pelvic venous pathology with DUS or other imaging tests is not recommended (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))

COMPRESSION THERAPY

- We advise **against** a 3-month trial of compression therapy prior to intervention in patients with symptomatic varicose veins who are candidates for **endovenous therapy** and wish to move on with treatment (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- With or without concurrent phlebectomy, we advise **post-procedure compression** therapy for a minimum of one week in patients receiving thermal ablation for saphenous incompetence (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))

PHARMACOLOGICAL TREATMENT

Table 5. Summary of the Pharmacologic Properties of Vasoactive Drugs Used for Chronic Venous Disorders

Venoactive drugs	Pharmacologic properties							
	Venous tone	Vein wall and valve	Capillary leakage	Lymphatic drainage	Hemorheological disorders	Antioxidant properties	Inflammatory reaction	Endothelial function
Micronized Purified Flavonoid Fraction (MPFF)	+	+	+	+	+	+	+	+
Ruscus extracts	+	+	+	+	+		+	
Hydroxyethylrutosides	+		+	+	+	+	+	
Calcium dobesilate	+		+	+	+	+		
Horse chestnut extract/escin	+		+			+		+
Red vine leaf extract			+			+		
Sulodexide							+	+

- Micronized Purified Flavonoid Fraction (**MPFF**) or Ruscus extracts are recommended for the treatment of vein-related pain, leg heaviness, and/or a feeling of swelling in symptomatic patients with varicose veins who are not candidates for intervention, are waiting for intervention, or have symptoms after intervention (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- **Hydroxyethylrutosides**, **Calcium Dobesilate**, **Horse Chestnut extract**, **red vine leaf extract**, or **Sulodexide** are recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))

FACTORS AFFECTING CHOICE OF SUPERFICIAL TRUNCAL ABLATION AND OUTCOME

- Selecting patients for venous ablation based on truncal vein diameter in symptomatic C2 disease patients is **not recommended** (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Prophylactic intervention does not stop venous disease progression in asymptomatic C2 disease patients. Compression stockings, avoiding prolonged standing, and controlling your weight **may all be helpful** (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Depending on the circumstances, a doctor who specializes in vein care may choose to treat varicose veins in a hospital operating room, a surgical center, or an office setting. Procedures carried out in an office setting were observed to provide better patient experiences and cheaper costs (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Isolated Sapheno-femoral junction (SFJ) incompetence in patients with symptomatic C2 disease **does not support** ablation of a GSV that is otherwise competent (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Even if the axial reflux is incomplete and the SFJ is competent, ablation of the incompetent GSV may be necessary in individuals with symptomatic C2 illness. Rarely is it necessary to ablate individual refluxing GSV segments when there are healthy segments nearby and farther away (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Ablation to the lowest point of reflux improved early outcomes in individuals with reflux in the below-knee GSV. In order to prevent thermal nerve injury, non-thermal procedures are preferable for the ablation of refluxing distal calf saphenous veins (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- **Thermal ablation** may result in skin burns, hyperpigmentation, or induration in patients with an epifascial or superficial saphenous vein, whereas non-thermal procedures may result in hyperpigmentation or induration. If the saphenous vein is close to the skin (<0.5 cm), mini-phlebectomy or restricted stripping is safe and efficient (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- **Thermal ablation** with EVLA or RFA should be used instead of non-thermal ablation procedures for patients with big (>10 mm), non-aneurysmal saphenous veins (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))

- **Both thermal and nonthermal ablations** have been observed to have a similar incidence of superficial thrombophlebitis (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Treatment of superficial incompetence is recommended first in patients with uncomplicated C2 illness (no venous claudication, thigh edema, suprapubic, or abdominal wall varicosities) caused by concurrent superficial incompetence and iliac or iliofemoral venous blockage (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))

INTERVENTIONS TO PRESERVE THE GSV

- If done by a doctor who is proficient in the ASVAL (ambulatory selective variceal ablation under local anesthesia) approach, sparing the GSV for patients with early-stage symptomatic varicose veins is **suggested** (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- If done by a doctor who is proficient in the **CHIVA** (Ambulatory Conservative Hemodynamic Correction of Venous Insufficiency) technique, sparing the GSV for patients with symptomatic varicose veins is suggested (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))

TREATMENT OF VENOUS TRIBUTARIES

- **Sclerotherapy with liquid or foam** for patients with reticular veins and telangiectasias that are symptomatic is recommended (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- If a patient has sclerosant allergy, needle phobia, sclerotherapy failure, or small veins (1mm) with telangiectatic matting, **transcutaneous laser treatment** for telangiectasias or reticular veins is suggested (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- **Mini-phlebectomy** or **ultrasound-guided sclerotherapy** using physician-compound foam (PCF) or polidocanol endovenous microfoam (PEM) are recommended for the treatment of symptomatic varicose tributaries (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- **Transilluminated powered phlebectomy** as an alternate treatment for patients with clusters of varicosities is suggested for the treatment of symptomatic varicose tributaries (Level of recommendation: grade 2 (week), quality of evidence: C (low to very low))

MANAGEMENT OF RECURRENT VARICOSITIES

- For patients with symptomatic recurrent varicosities, clinical evaluation and DUS **should be performed** before treatment to determine the potential source of recurrence (Level of recommendation: ungraded good clinical practice)
- For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux of the GSV or AAGSV, treatment either with **open surgical or endovascular techniques** may be performed, with good outcomes expected (Level of recommendation: ungraded good clinical practice)
- For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux at the groin, either **EVLA or RFA** can be used if there is a straight GSV stump, long enough for thermal ablation. Sclerotherapy or phlebectomy should be performed for recurrence due to neovascularization (Level of recommendation: ungraded good clinical practice)
- For patients with symptomatic recurrent varicosities due to persistent or recurrent reflux of the SSV, ultrasound-guided foam sclerotherapy should be performed (Level of recommendation: ungraded good clinical practice)
- For patients with residual or recurrent varicosities due to incompetent perforator veins, treatment with both open and endovascular techniques may be used depending on the physician's experience, patient choice and availability of technology (Level of recommendation: ungraded good clinical practice)

MANAGEMENT OF ABLATION RELATED THROMBUS EXTENSION (ARTE) AND DEEP VEIN THROMBOSIS (DVT) AFTER ENDOVENOUS ABLATIONS

- Routine early post-procedural DUS to identify **ablation-related thrombus extension** (ARTE, technically known as Endovenous Heat Induced Thrombosis, EHIT) or **DVT** is not recommended in an average-risk patient who is asymptomatic after thermal ablation of the saphenous vein (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- In a **high-risk patient** who is asymptomatic following thermal or non-thermal saphenous ablation early DUS to exclude ablation-related thrombus extension (ARTE) or DVT should be performed (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- **Early DUS** in patients who experience symptoms after thermal or non-thermal ablation is recommended in order to rule out DVT or ablation-related thrombus extension (ARTE) (Level of recommendation: grade 1 (strong), quality of evidence: A (high))

- **Pharmaceutical thromboprophylaxis** is suggested for high-risk individuals having endovenous ablation (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- Serial deep vein imaging for **two weeks** is advised in individuals with acute isolated distal DVT following varicose vein surgery who have no symptoms or risk indicators for extension (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))
- Patients with isolated distal DVT following varicose vein surgery with symptoms or extension risk factors are advised to take **anticoagulation** (Level of recommendation: grade 2 (weak), quality of evidence: C (low to very low))
- **Direct oral anticoagulants** over vitamin K antagonists are recommended for patients with acute proximal DVT following varicose vein surgery (Level of recommendation: grade 1 (strong), quality of evidence: B (moderate))
- **Direct oral anticoagulants** over vitamin K antagonists are recommended for patients with symptomatic ARTE following endovenous ablation (Level of recommendation: grade 1 (strong), quality of evidence: C (low to very low))

MANAGEMENT OF SUPERFICIAL VEIN THROMBOSIS (SVT)

- We advise **fondaparinux 2.5mg** subcutaneously daily for 45 days for individuals with Superficial Vein Thrombosis (SVT) of the main saphenous trunks and tributaries above the knee that are > 3 cm from the SFJ and > 5 cm in length, whether or not varicose veins are present. Alternatively, people who are unable or reluctant to administer subcutaneous injections may benefit from taking **rivaroxaban** 10mg once daily for 45 days (Level of recommendation: grade 1 (strong), quality of evidence: A (high))
- Utilizing **prophylactic or therapeutic doses** of LMWH and NSAIDs for patients with SVT of the major saphenous trunks is not recommended. Both have been shown to lessen SVT pain and extension, but they haven't been able to stop VTE. Due to the high prevalence of concurrent DVT, surveillance with DUS for VTE extension is advised if NSAIDs are used to treat short segment distal SVT ablation (Level of recommendation: grade 1 (strong), quality of evidence: A (High))
- **Phlebectomy** is recommended as a safe alternative for some individuals with isolated thrombosis of varicose tributaries or mild GSV involvement ablation (Level of recommendation: grade 2 (weak), quality of evidence: B (moderate))

MANAGEMENT OF BLEEDING VARICOSE VEINS

- For patients presenting with **acute bleeding** from varicose veins, leg elevation, direct compression and sclerotherapy should be attempted before suture ligation to control bleeding (Level of recommendation: ungraded good clinical practice)
- For patients who presented with **bleeding** from varicose veins, after the bleeding has been controlled, evaluation for superficial venous incompetence and appropriate intervention on the responsible veins should be done to control venous hypertension and reduce the risk of recurrent hemorrhage (Level of recommendation: ungraded good clinical practice)

MANAGEMENT OF SUPERFICIAL VEIN ANEURYSMS

- For patients with **superficial truncal vein aneurysm**, located within 3 cm of the SFJ or saphenopopliteal junction (SPJ), open surgical excision, with high proximal and distal ligations should be performed. If symptomatic saphenous reflux is present, endovenous or open surgical ablation (phlebectomy or limited stripping) of the distal saphenous vein should be performed (Level of recommendation: ungraded good clinical practice)
- Patients with symptomatic, thrombosed or large (> 3cm) aneurysms in the superficial veins are best treated with **surgical excision** (Level of recommendation: ungraded good clinical practice)

1.2 European Guidelines

1.2.1 NICE Guidelines for the Diagnosis and Management of Varicose Veins (2013)

The guidelines published by the National Institute for Health Care Excellence (NICE) in 2013 cover the diagnosis and management of varicose veins in people aged 18 and over. It aims to ensure that people understand the options for treating varicose veins and that healthcare professionals know when to refer people for specialist assessment and treatment[10].

Information for people with varicose veins

Give those who exhibit varicose veins the following information:

- What varicose veins are.
- Varicose vein reasons that may exist.

- the chance of development and potential side effects, such as thrombophlebitis, deep vein thrombosis, skin abnormalities, leg ulcers, bleeding, and alterations in appearance.
- Options for treatment include symptom relief, a description of interventional procedures, and the function of compression.
- Advice on:
    - ✓ Weight loss
    - ✓ Light to moderate physical activity
    - ✓ Avoiding factors that are known to make their symptoms worse if possible
    - ✓ When and where to seek further medical help.

Tell the patient the following while discussing varicose vein treatment at the vascular service:

- What choices there are for treatment.
- The anticipated advantages and dangers of any available treatment.
- That following treatment, additional varicose veins could appear.
- That they might require more than one treatment session
- That recurrent varicose veins have a larger likelihood of returning following therapy than do primary varicose veins.

Assessment

- For those who have suspected primary or recurrent varicose veins, it is recommended to use **duplex ultrasonography** to confirm the diagnosis, determine the severity of truncal reflux, and arrange treatment.

Interventional treatment

- For people with confirmed varicose veins and truncal reflux:
    - Offer **endothermal ablation**.
    - If endothermal ablation is unsuitable, offer **ultrasound-guided foam sclerotherapy.**
    - If ultrasound-guided foam sclerotherapy is unsuitable, offer **surgery**.
- Consider treating ineffective varicose tributaries simultaneously if you must.
- **Compression bandaging** or hosiery should not be used longer than 7 days after interventional treatment.

- Current evidence on the safety and efficacy of **radiofrequency ablation** of varicose veins appears adequate to support the use of this procedure as an alternative to saphenofemoral ligation and stripping, provided that the normal arrangements are in place for consent, audit and clinical governance.
- Current evidence on the safety and efficacy of **endovenous laser treatment** of the long saphenous vein appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. Current evidence on the efficacy of this procedure is limited to case series with up to 3 years follow-up. Clinicians are encouraged to collect longer-term follow-up data.
- Current evidence on the efficacy of **ultrasound-guided foam sclerotherapy** for varicose veins is adequate. The evidence on safety is adequate, and provided that patients are warned of the small but significant risks of foam embolisation, this procedure may be used with normal arrangements for clinical governance, consent and audit.

Non-interventional treatment

- Unless interventional treatment is inappropriate, avoid recommending **compression** hosiery for the treatment of varicose veins.

Management during pregnancy

- Pregnant women who have varicose veins should be informed on how pregnancy affects veinous insufficiency.
- **Interventional therapy** for varicose veins should not be done during pregnancy unless absolutely necessary.
- **Compression hosiery** are recommended for symptom relief of leg swelling brought on by varicose veins during pregnancy.
- Refer people to a vascular service if they have any of the following:
    - Main or recurring varicose veins with symptoms. Veins that are associated with bothersome lower limb symptoms, such as pain, aching, discomfort, swelling, heaviness, and itching, are referred to as symptomatic veins
    - Skin abnormalities in the lower limbs, including eczema and pigmentation, are thought to be brought on by chronic venous insufficienc
    - Possible venous incompetence and superficial vein thrombosis, which is characterized by the presence of painful, hard veins

- A skin break below the knee that has not healed after two weeks is known as a venous leg ulcer
- A recovered venous leg ulcer
- Bleeding varicose veins.

1.2.2 ESVS Clinical Practice Guidelines on the Management of Chronic Venous Disease of the Lower Limbs (2022)

The focus of the European Society for Vascular Surgery (ESVS) published in 2022 is on chronic venous disease (CVD) of the lower limbs, related to pathology of the superficial, perforating and deep veins of the lower limbs as well as to abdominal and pelvic venous pathology. The guidelines report several recommendations on diagnosis and treatment of varicose veins in different chapters[11].

Scoring systems

- For clinical audit and research, it is advised to utilize the Clinical, Etiological, Anatomical, Pathophysiological (**CEAP**) categorization for patients with chronic venous illness (Class of recommendation: I; Level of evidence: C)
- For clinical audit and research, it is recommended that patients with chronic venous disease have their clinical severity and treatment outcomes assessed using the revised Venous Clinical Severity Score (r-**VCSS**) and the **Villalta scale** for post-thrombotic syndrome (Class of recommendation: IIa; Level of evidence: C)

Table 6. The 2020 Update of CEAP: Summary of Anatomical Classification (Retrieved from the ESVS 2022 Guidelines)

Anatomical classification	Segment number*	New anatomical site†	Description
As (Superficial)	1	Tel	Telangiectasia
	1	Ret	Reticular veins
	2	GSVa	Great saphenous vein, above knee
	3	GSVb	Great saphenous vein, below knee
	4	SSV	Small saphenous vein
	–	AASV	Anterior accessory saphenous vein
	5	NSV	Non-saphenous vein
Ad (Deep)	6	IVC	Inferior vena cava
	7	CIV	Common iliac vein
	8	IIV	Internal iliac vein
	9	EIV	External iliac vein
	10	PELV	Pelvic vein
	11	CFV	Common femoral vein
	12	DFV	Deep femoral vein
	13	FV	Femoral vein
	14	POPV	Popliteal vein
	15	TIBV	Crural (Tibial) vein
	15	PRV	Peroneal vein
	15	ATV	Anterior tibial vein
	15	PTV	Posterior tibial vein
	16	MUSV	Muscular veins
	16	GAV	Gastrocnemius vein
	16	SOV	Soleal vein
Ap (Perforator)	17	TPV	Thigh perforator vein
	18	CPV	Calf perforator vein
An (No venous anatomic location identified)			

Table 7. The Revised Venous Clinical Severity Score (r-VCSS) (Retrieved from the ESVS 2022 Guidelines)

Variable	Description (score)			
	Absent (0)	Mild (1)	Moderate (2)	Severe (3)
Pain* or ulcer discomfort	None	Occasional	Daily, interfering with, but not preventing regular activities	Daily, limiting most regular activities
Varicose veins	None	Few, scattered or corona phlebectatica	Confined to calf or thigh	Involve calf and thigh
Venous oedema	None	Limited to foot or ankle	Extends above ankle but below knee	Extends to knee or above
Skin pigmentation	None or focal	Limited to perimalleolar area	Diffuse over lower third of calf	Wider distribution (above lower third of calf)
Inflammation	None	Limited to perimalleolar area	Diffuse over lower third of calf	Wider distribution (above lower third of calf)
Induration	None	Limited to perimalleolar area	Involving lower third of calf	Involving more than lower third of calf
Number of active ulcers	None	1	2	> 2
Active ulcer duration	None	< 3 mo	> 3 mo but < 1 y	> 1 y
Active ulcer size	None	Diameter < 2 cm	Diameter 2–6 cm	Diameter > 6 cm
Compression therapy	Not used	Intermittent use of stocking	Stocking use most days	Full compliance with stockings

* Ache, heaviness, fatigue, soreness, and burning presumptive of a venous origin.

Table 8. The Villalta Scale and its Interpretation for Post-Thrombotic Syndrome (PTS) (Retrieved from the ESVS 2022 Guidelines)

Clinical findings*	None	Mild	Moderate	Severe
Symptoms				
Pain	0	1	2	3
Cramping	0	1	2	3
Heaviness	0	1	2	3
Pruritis	0	1	2	3
Paraesthesia	0	1	2	3
Signs				
Oedema	0	1	2	3
Induration	0	1	2	3
Hyperpigmentation	0	1	2	3
Venous ectasia	0	1	2	3
Redness	0	1	2	3
Calf tenderness	0	1	2	3
Interpretation of severity of post thrombotic syndrome				
Villalta score	< 5	5–9	10–14	> 14 or the presence of venous ulceration

* Each variable is given a score of between 0 and 3 indicative of a severity of none, mild, moderate, or severe, respectively, with a maximum score of 33.

Investigations

- Full lower limb venous **duplex ultrasonography** is advised as the primary imaging modality for diagnostic and therapy planning in individuals with suspected or clinically evident chronic venous illness (Class of recommendation: I; Level of evidence: B)
- Air **plethysmography** can be used for patients with chronic venous illness to quantify reflux and/or obstruction, particularly when duplex ultrasonography results do not agree with the clinical findings (Class of recommendation: IIb; Level of evidence: C)
- For patients with suspected supra-inguinal venous obstruction, in addition to full leg duplex assessment, **ultrasound** of the abdominal and pelvic veins should be considered, as part of the initial assessment (Class of recommendation: IIa; Level of evidence: C)
- When an intervention is contemplated in patients with suspected supra-inguinal venous obstruction, cross sectional imaging by **magnetic resonance venography or computed tomography** is recommended in addition to duplex ultrasound assessment (Class of recommendation: I; Level of evidence: C)
- For selected patients with suspected supra-inguinal venous obstruction, where cross sectional diagnostic imaging is inadequate or not available, **venography and/or intravascular ultrasound** may be considered (Class of recommendation: IIb; Level of evidence: B)

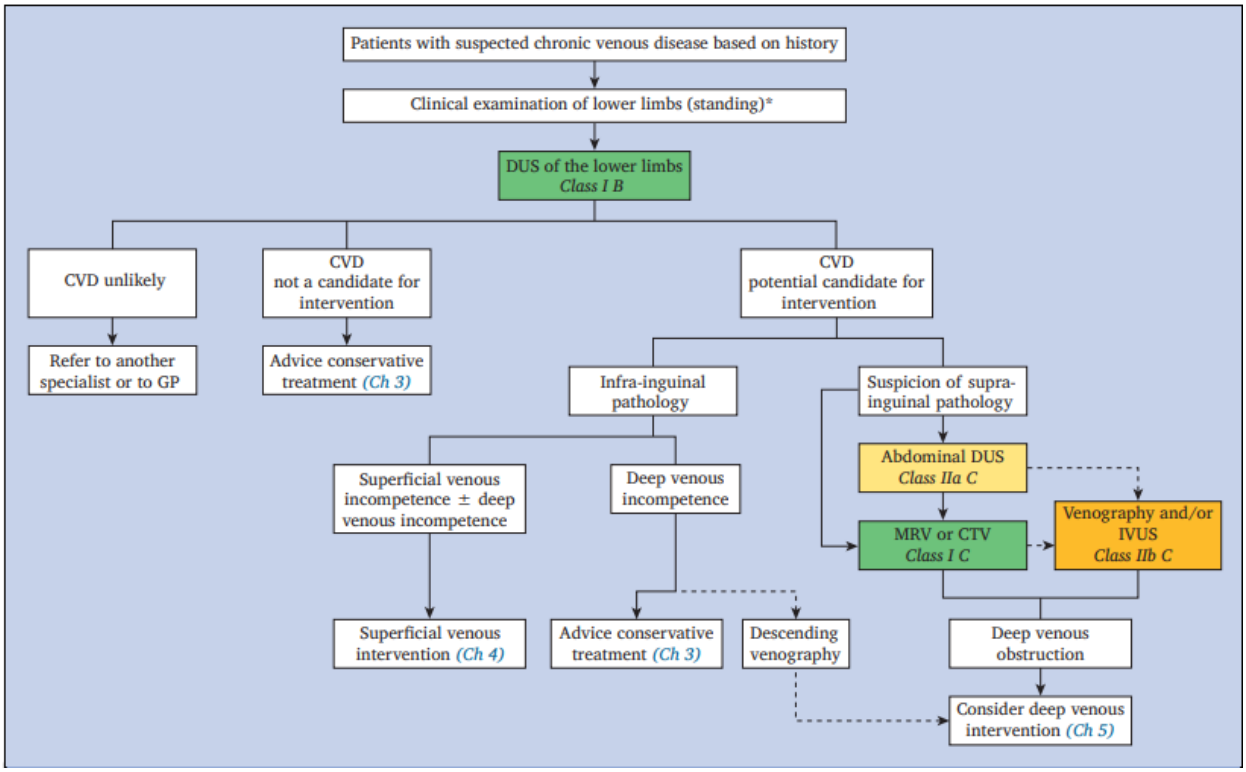


Figure 3. *Main Diagnostic Pathways for Patients with Suspected Chronic Venous Disease of the Lower Limbs and Main Treatment Pathways (Retrieved from the ESVS 2022 Guidelines)*

Compression therapy

- **Exercise** should be taken into consideration for people with symptomatic chronic venous illness in order to lessen venous symptoms (Class of recommendation: IIa; Level of evidence: B)
- **Elastic compression** stockings that apply pressure of at least 15 mmHg at the ankle are advised for individuals with symptomatic chronic venous illness in order to lessen venous symptoms (Class of recommendation: I; Level of evidence: B)
- **Compression therapy**, employing below-knee elastic compression stockings, inelastic bandages, or adjustable compression garments, exerting a pressure of 20 to 40 mmHg at the ankle, is advised for patients with chronic venous disease and oedema (CEAP clinical class C3) (Class of recommendation: I; Level of evidence: B)
- To lessen skin induration, it is advised for patients with chronic venous disease and lipodermatosclerosis, and/or atrophie blanche (CEAP clinical class C4b) to use below-knee elastic **compression stockings** that impose a pressure of 20 to 40 mmHg at the ankle (Class of recommendation: I; Level of evidence: B)

Table 9. Contraindications to Compression Treatment

Contraindications to compression treatment
Severe lower extremity atherosclerosis disease with ABI<0.6 and/or ankle pressure < 60 mmHg
Extra-anatomic or superficially tunneled arterial bypass at the site of intended compression
Severe heart failure, NYHA class IV
Heart failure NYHA class III and routine application of compression devices without clinical and hemodynamic monitoring
Confirmed allergy to compression material
Severe diabetic neuropathy with sensory loss or microangiopathy with the risk of skin necrosis

Pharmacotherapy

- Based on the available research for each individual drug, medical treatment with **venoactive drugs** should be taken into consideration for patients with symptomatic chronic venous disease who cannot receive interventional treatment, are waiting for intervention, or have symptoms and/or oedema that persist after intervention (Class of recommendation: IIa; Level of evidence: A)

Table 10. Global Summary of the Effects of the Main Venoactive Drugs on Venous Symptoms and Edema

Symptoms or sign	Venoactive Drugs						
	Ruscus extracts	MPFF	Calcium dobesilate	Horse chestnut extract	Hydroxyethyl-rutosides	Red vine leaf extract	Sulodexide
Pain	+	+	+	+	+	+	+
Heaviness	+	+	+		+		+
Fatigue	+		+				
Feeling of swelling	+	+					+

Cramps	+	+	+		+		+
Paresthesia	+	+	+				
Pruritis			+	+			
Oedema	+	+	+	+		+	

Figure 4 details an algorithm for the conservative management of CVD of the lower limbs.

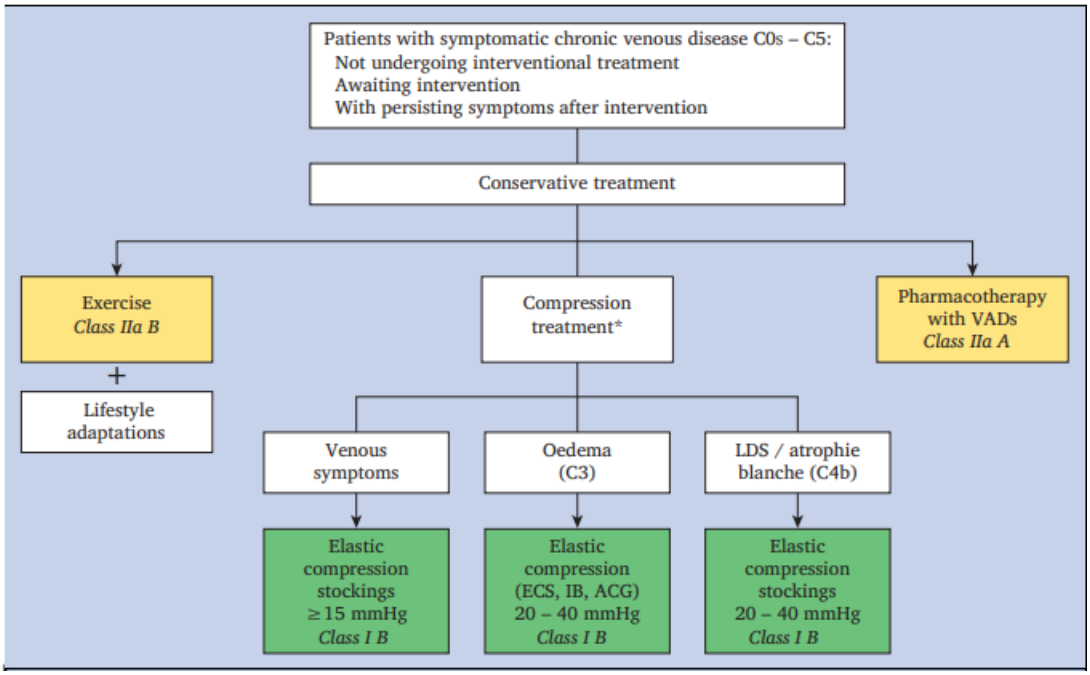


Figure 4. *Conservative Management of Patients with Chronic Venous Disease of the Lower Limbs (Retrieved from the ESVS 2022 Guidelines)*

Interventional therapy

- **Interventional therapy** is recommended for individuals with superficial venous incompetence who present with symptomatic varicose veins (CEAP clinical class C2S) (Class of recommendation: I; Level of evidence: B)
- Before deciding on interventional treatment for patients with superficial venous incompetence who present with oedema (CEAP clinical class C3), additional non-venous sources of oedema should be taken into account (Class of recommendation: IIa; Level of evidence: C)
- Interventional treatment for superficial venous incompetence is advised for patients who present with skin abnormalities as a result of chronic venous

illness (CEAP clinical class C4 or C6) (Class of recommendation: I; Level of evidence: C)

- When possible, treatments for patients with superficial venous incompetence who are receiving **endovenous therapy** with or without phlebectomies should be carried out in an outpatient setting (Class of recommendation: I; Level of evidence: C)
- **Ultrasound guided tumescent anesthesia** is recommended for patients with superficial venous incompetence who are receiving endovenous thermal ablation treatment (Class of recommendation: I; Level of evidence: C)
- **Buffering solutions** should be taken into consideration for individuals with superficial venous incompetence receiving tumescent anesthesia in order to lessen peri-procedural pain (Class of recommendation: IIa; Level of evidence: B)
- As an alternative to general or regional anesthesia, ultrasound guided tumescent anesthesia may be used for patients with superficial venous incompetence undergoing high ligation/stripping (Class of recommendation: IIb; Level of evidence: C)
- **Postprocedural compression** therapy should be taken into consideration for patients with superficial venous incompetence receiving ultrasound guided foam sclerotherapy or endovenous thermal ablation of a saphenous trunk (Class of recommendation: IIa; Level of evidence: A)
- **Immediate post-procedural compression** therapy is advised for patients with superficial venous incompetence following stripping and/or severe phlebectomies (Class of recommendation: I; Level of evidence: A)
- The length of post-intervention compression, which is utilized to reduce post-operative local problems in patients with superficial venous incompetence, should be determined on an individual basis (Class of recommendation: I; Level of evidence: A)
- Risk assessment for **venous thromboembolism** is recommended for patients with superficial venous incompetence receiving treatment (Class of recommendation: I; Level of evidence: C)
- **Individualized thromboprophylaxis** techniques for individuals with superficial venous incompetence undergoing intervention should be taken into account (Class of recommendation: IIa; Level of evidence: B)
- One to four weeks after saphenous trunk therapy, duplex **ultrasonography** surveillance should be taken into consideration for patients with superficial venous incompetence (Class of recommendation: IIa; Level of evidence: C)

- **Endovenous thermal ablation** is recommended as a first-choice treatment for patients with great saphenous vein incompetence who need to be treated, instead of high ligation/stripping and ultrasound-guided foam sclerotherapy (Class of recommendation: I; Level of evidence: A)
- The choice of the device for individuals having thermal ablation who have saphenous trunk superficial venous incompetence should be left up to the treating physician's judgment (Class of recommendation: I; Level of evidence: B)
- When a non-thermal non-tumescent approach is selected, **cyanoacrylate adhesive** closure should be taken into consideration for individuals with superficial venous incompetence of a saphenous trunk who need therapy (Class of recommendation: IIa; Level of evidence: A)
- For the treatment of saphenous trunks with a diameter less than 6 mm in patients with superficial venous incompetence, ultrasonography guided foam sclerotherapy should be taken into consideration (Class of recommendation: IIB; Level of evidence: B)
- For patients with superficial venous incompetence treated with **foam sclerotherapy**, the procedure should be performed under ultrasound guidance (Class of recommendation: I; Level of evidence: C)
- Patients who need treatment for superficial venous incompetence of the saphenous trunk may be candidates for **catheter-directed foam sclerotherapy**, either with or without the use of peri-venous tumescent solution (Class of recommendation: IIb; Level of evidence: B)
- **Mechanochemical ablation** may be an option for patients who need therapy for superficial venous incompetence of a saphenous trunk if a non-thermal non-tumescent method is selected (Class of recommendation: IIb; Level of evidence: A)
- If **endovenous thermal ablation** treatments are not accessible for individuals with great saphenous vein incompetence who need therapy, high ligation/stripping should be taken into consideration (Class of recommendation: IIa; Level of evidence: A)
- Patients with chronic venous illness who need to treat varicose tributaries are advised to undergo an **ambulatory phlebectomy**, ultrasound-guided foam sclerotherapy, or a combination of the two (Class of recommendation: I; Level of evidence: B)
- **Endovenous ablation, division, or ligation** should be taken into consideration for treating incompetent perforating veins in individuals with chronic venous illness (Class of recommendation: IIa; Level of evidence: C)

- Prior to treatment, a **duplex ultrasound** of the lower extremity veins should be conducted on patients who have reticular veins and/or telangiectasias to check for any associated incompetent veins (Class of recommendation: I; Level of evidence: C)
- Prior to treating smaller veins in patients who have reticular veins and/or telangiectasias, major **accompanying incompetent** veins should be addressed (Class of recommendation: I; Level of evidence: C)
- **Sclerotherapy** is recommended as the first line of treatment for patients with reticular veins for whom treatment is planned (Class of recommendation: I; Level of evidence: A)
- **Sclerotherapy** should be taken into consideration for patients with telangiectasias if treatment is planned Class of recommendation: IIa; Level of evidence: A)
- **Transcutaneous laser** should be taken into consideration for patients with telangiectasias who are scheduled for treatment (Class of recommendation: IIa; Level of evidence: B)
- **Endovenous thermal ablation** is recommended over surgery or foam sclerotherapy for patients who need treatment for small saphenous vein incompetence (Class of recommendation: I; Level of evidence: A)
- Endovenous non-thermal non-tumescent ablation techniques may be considered for patients who need therapy for small saphenous vein incompetence (Class of recommendation: IIb; Level of evidence: B)
- If cannulation is performed below midcalf level on patients with minor saphenous vein incompetence receiving endovenous thermal ablation, care should be taken to prevent sural nerve injury (Class of recommendation: I; Level of evidence: B)
- **Endovenous thermal ablation** should be taken into consideration for patients who require therapy for anterior accessory saphenous vein incompetence (Class of recommendation: IIa; Level of evidence: C)
- The use of **ultrasound-guided foam sclerotherapy** may be an option for patients who need treatment for anterior accessory saphenous vein incompetence (Class of recommendation: IIb; Level of evidence: C)
- **Concomitant** tributary treatment should be taken into account for patients with an incompetent saphenous trunk who are being treated with endovenous thermal or non-thermal ablation as part of a collaborative decision process (Class of recommendation: IIa; Level of evidence: B)

- Treatment of incompetent lower leg perforating veins is not advised for the majority of varicose vein patients without skin abnormalities linked to chronic venous illness (Class of recommendation: III; Level of evidence: C)
- Treatment options may be investigated for individuals with considerable isolated or residual incompetent perforating veins and progressive skin alterations (CEAP clinical classes C4b, C5 or C6) (Class of recommendation: IIb; Level of evidence: C)
- Ambulatory conservative hemodynamic therapy of venous incompetence (**CHIVA**), when done by medical professionals, may be considered for patients with superficial venous incompetence who need treatment (Class of recommendation: IIb; Level of evidence: B)
- **Phlebectomies** with preservation of the saphenous trunk (ASVAL) may be a treatment option for people with uncomplicated varicose veins (CEAP clinical class C2) (Class of recommendation: IIb; Level of evidence: C)
- **Endovenous thermal ablation** should be taken into consideration for patients who have an incompetent great saphenous vein with a very large truncal diameter (greater than 12 mm) (Class of recommendation: IIa; Level of evidence: C)
- **Phlebectomy, sclerotherapy, and foot perforating vein ligation** may be considered during or following proximal reflux ablation for patients who present with foot and ankle varicose veins (Class of recommendation: IIb; Level of evidence: C)
- **Endovenous thermal ablation** or ultrasound-guided foam sclerotherapy with or without phlebectomy should be taken into consideration for individuals with symptomatic recurrent varicose veins caused by saphenous trunk incompetence Class of recommendation: IIa; Level of evidence: B)
- Re-exploration of the groin or popliteal fossa is not advised for individuals with symptomatic recurrent varicose veins who need treatment and where endovenous ablation is available Class of recommendation: III; Level of evidence: B)
- **Ultrasound guided foam sclerotherapy** and/or ambulatory phlebectomy should be taken into consideration for individuals with symptomatic recurrent varicose veins without truncal incompetence (Class of recommendation: IIa; Level of evidence: C)

Table 11. Main Causes of Varicose Vein Recurrence After Treatment

Cause	Description
Tactical error	Persistence of reflux because of an inappropriate intervention: - Inadequate pre-operative DUS, not identifying the source(s) of reflux - Inadequate choice of cannulation site(s)
Technical error	Persistence of reflux because of inadequate intervention For endovenous procedures: - Failure to cannulate target saphenous trunk - poor ultrasound visualization of the target segment, the SFJ, or the SPJ - insufficient delivery of energy/glue/sclerosant to target segment For open surgical procedures: - Incomplete stripping - Other surgical failure
Neovascularization	Presence of multiple new small tortuous refluxing veins in anatomical proximity to a previous intervention: - Reflux from a previously ligated or ablated SFJ, SPJ, PV, or tributary - New veins visible on DUS in connection with varicose veins
Recanalization	Partial or complete reopening of an initial ablated saphenous segment with recurrence of reflux
Disease progression	Development of venous reflux as a result of the natural history and progression of disease, with reflux occurring at new sites

- Treatment of incompetent superficial veins should be taken into consideration in patients with chronic venous illness brought on by both superficial and deep venous incompetence (Class of recommendation: IIa; Level of evidence: C)
- **Specific duplex ultrasound screening** of pelvic escape sites is advised for individuals who report with symptomatic varicose veins that may have a pelvic origin (Class of recommendation: I; Level of evidence: C)

- **Local therapies** for varicose veins and associated pelvic escape sites may be taken into consideration as the initial therapeutic method for individuals with pelvic origin varicose veins who do not have pelvic symptoms needing therapy (Class of recommendation: IIa; Level of evidence: C)
- **Pelvic vein embolization** should not be used as the first course of treatment for patients with varicose veins of the pelvic origin who do not have pelvic symptoms (Class of recommendation: III; Level of evidence: C)
- **Pelvic vein embolization** should be taken into consideration to alleviate symptoms in symptomatic patients with varicose veins of the pelvis who need therapy for pelvic discomfort (Class of recommendation: IIa; Level of evidence: B)
- **Local foam sclerotherapy** should be taken into consideration for individuals with chronic venous illness who have experienced an episode of acute bleeding from superficial veins or telangiectasias in order to stop recurring bleeding (Class of recommendation: IIa; Level of evidence: C)
- For patients with chronic venous disease, who are obese, **weight loss** should be considered for improving venous outcomes (Class of recommendation: IIa; Level of evidence: C)
- For obese patients with superficial venous incompetence of a saphenous trunk requiring treatment, **endovenous ablation** should be considered (Class of recommendation: IIa; Level of evidence: C)
- The use of **elastic compression hosiery** is recommended for pregnant women exhibiting symptoms and/or indicators of chronic venous illness (Class of recommendation: I; Level of evidence: B)
- **Anticoagulation** should not be stopped in patients with chronic venous illness who are scheduled to have endovenous thermal ablation and who are taking anticoagulants (Class of recommendation: III; Level of evidence: C)

Figures 5, 6, and 7 detail treatment options for the management of patients with symptomatic great saphenous vein (GSV) incompetence, symptomatic small saphenous vein (SSV) incompetence, and symptomatic anterior accessory saphenous vein (AASV) incompetence respectively.

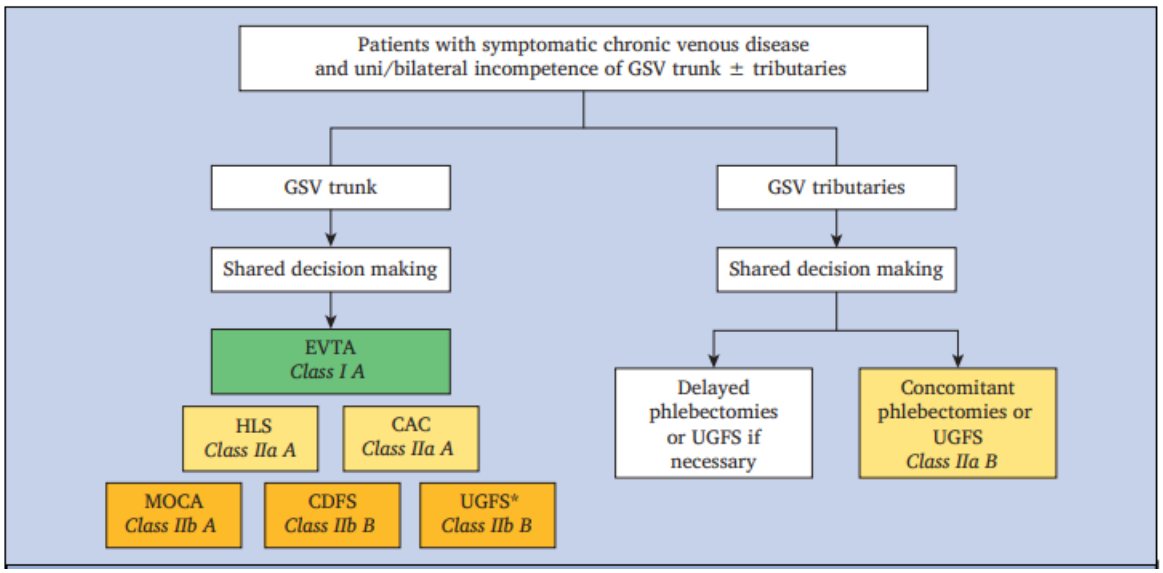


Figure 5. *Interventional Treatment Options for Patients with Symptomatic Great Saphenous Vein (GSV) Incompetence (Retrieved from the 2022 ESVS Guidelines)*

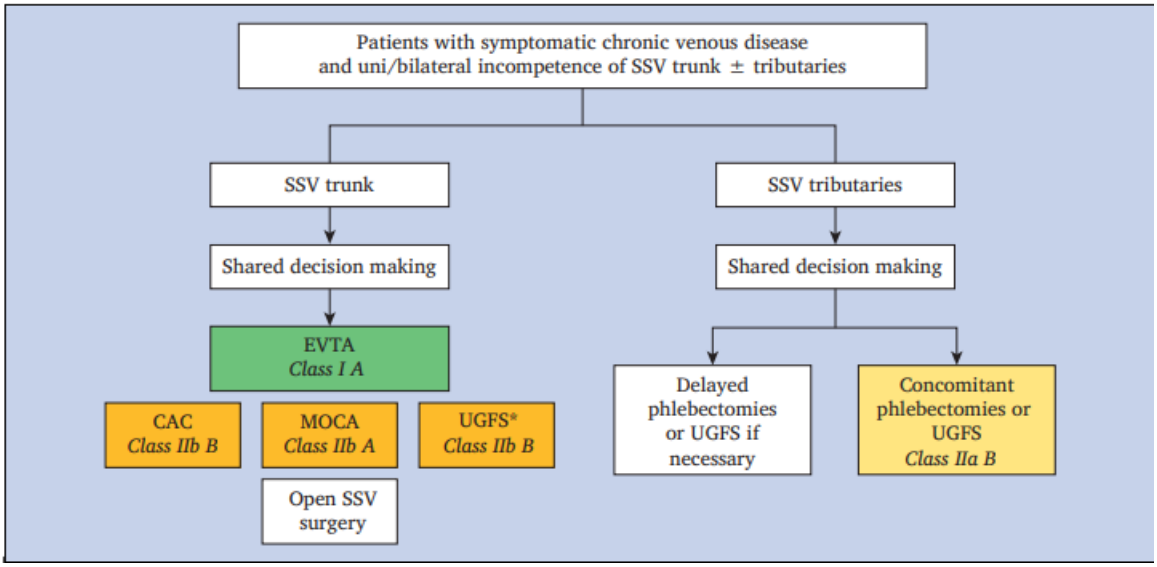


Figure 6. *Interventional Treatment Options for Patients with Symptomatic Small Saphenous Vein (SSV) Incompetence (Retrieved from the ESVS 2022 Guidelines)*

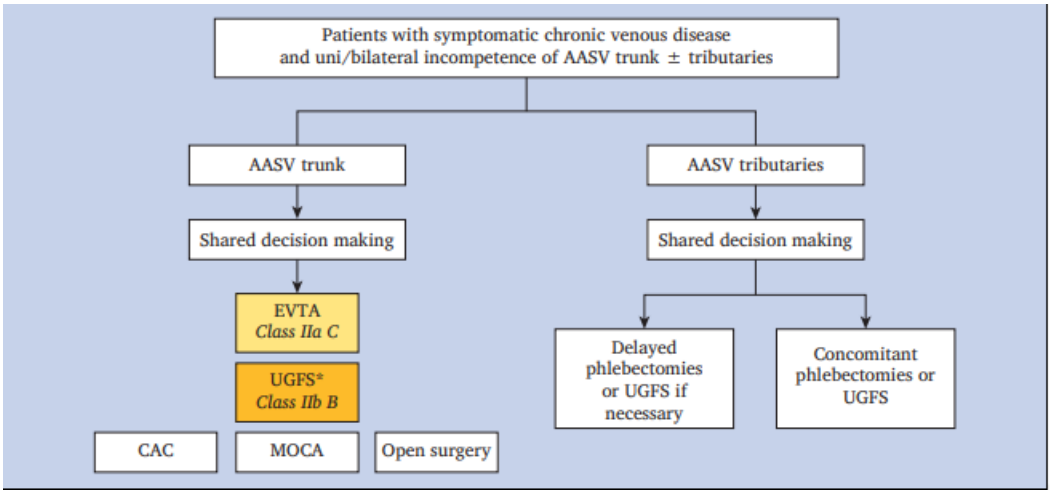


Figure 7. *Interventional Treatment Options for Patients with Symptomatic Anterior Accessory Saphenous Vein (AASV) Incompetence (Retrieved from the ESVS 2022 Guidelines)*

1.2.3 S2k Guidelines for the Diagnosis and Treatment of Varicose Veins (2022)

The S2k guidelines were published in 2022 by the Association of the Scientific Medical Societies in Germany. These guideline deal with the diagnosis and treatment of subcutaneous varicose veins and intrafascial varicose veins[12].

Classification and explanations given to the patients

- A special **evaluation** should be performed in the case of a symptomatic or severe varicose vein in order to plan additional procedures. In order to achieve this, the patient should be sent to a vein expert who is sufficiently knowledgeable about the whole range of diagnoses, including duplex ultrasonography, and the range of potential therapies and/or may provide useful advice. (Level of recommendation: moderate)
- A **vein expert** should be seen for further treatment planning if a patient has varices during pregnancy, superficial vein thrombosis, variceal bleeding, or a venous leg ulcer. (Level of recommendation: strong)
- Both **conservative and invasive methods** can be used to treat varicose veins and their consequences. The patient's preferences, the extent and location of the pathological changes to the superficial and deep vein systems, and the patient's overall health all influence the treatment plan. (Level of recommendation: weak)
- A **hemodynamically** efficient treatment must be explored for people who have varicose veins and symptoms of CVI (venous oedema to venous leg ulcer). (Level of recommendation: strong)

- Suitable treatment must be sought in the case of varicose vein complications (variceal hemorrhage, superficial vein thrombosis, venous leg ulcer). (Level of recommendation: strong)
- The severity of a varicose vein can be determined using **quality-of-life assessments and clinically validated scores.** (Level of recommendation: weak)
- The explanations and technique of therapy selection must take into account the patient's preferences. They play a significant role in the choice of treatment. (Level of recommendation: strong)
- The explanatory **conversation** shall discuss the type, severity, possible complications, and prognosis of the clinical picture. The different treatment options shall be explained, with their advantages and potential risks. (Level of recommendation: strong)
- Patients must be made aware of the fundamentals, the efficacy, and any potential side effects of the recommended treatment, as well as any potential insurance coverage options. (Level of recommendation: strong)
- The explanation should point out that venous disorders generally worsen over time and that long-term, conservative, symptom-focused treatment is usually necessary. (Level of recommendation: moderate)

Table 12. Clinical Classification (C) According to CEAP

Class	Clinical signs
C_0	No visible or palpable signs of venous incompetence
C_1	Spider veins and/or reticular varices
C_2	Varicose veins
C_3	Oedema
C_{4a}	Pigmentation, eczema
C_{4b}	Atrophie blanche, dermatoliposclerosis
C_5	Cured venous leg ulcer
C_6	Active venous leg ulcer

Diagnosis

- The decision for a diagnosis that will guide further action will be based on an assessment of the patient's medical file and a clinical examination. (Level of recommendation: strong)

- In the framework of standardized phlebological diagnosis, an imaging approach shall be applied. **Duplex ultrasonography** is to be used as the first option. Vein function must also be assessed, using tools like PPG/LRR or VOP, if necessary. (Level of recommendation: strong)
- The clinical examination shall be taken into the treatment decision consideration as appropriate, as it reflects the severity of the disease. (Level of recommendation: strong)
- **Photoplethysmography** (PPG, LRR) can be used as a screening procedure to quantify venous function and/or to regulate evolution. (Level of recommendation: weak)
- An indication for invasive therapy cannot be made only on the basis of a CW Doppler ultrasonography analysis. (Level of recommendation: strong)
- Differentiated indications for treating varicose veins must be based on the results of a duplex ultrasonography. It should also be utilized for examinations following invasive varicose vein therapy. (Level of recommendation: strong)
- Parallel diagnosis with duplex ultrasonography is required when doing endovenous varicose vein therapy. (Level of recommendation: strong)
- **Clinical examination** of varicose veins and duplex ultrasound evaluation of the vein system should be carried out with the patient standing up. (Level of recommendation: moderate)
- Prior to varicose vein therapy, computed tomography and magnetic resonance phlebography should not be employed for the initial diagnosis. (Level of recommendation: strong)

Table 13. Objects of Diagnosis of Varicose Veins

The objects of diagnosis of a varicose vein disease are as follows
Discovery and classification of the hemodynamic disturbance (duplex ultrasound)
Classification of the medical significance (medical record, inspection, duplex ultrasound, light reflection rheography [LRR], venous occlusion plethysmography [VOP])
Differentiation of a primary from a secondary varicose vein (duplex ultrasound, occasionally other imaging techniques, LRR, VOP)
Discovery and classification of the deep vein system (duplex ultrasound, phlebography, other imaging techniques, LRR, VOP)
Follow-up for quality control after the intervention (medical record, inspection, duplex ultrasound, LRR, VOP)

Analysis of recurrence (cause, extent) (duplex ultrasound, inspection)

Varicose vein treatment

- The best course of treatment for each patient with symptomatic chronic vascular disease should always be chosen individually. Invasive treatments, compression therapy, and drug-based treatment are not alternatives that are in competition with one another but rather work well together when appropriate (Level of recommendation: moderate)
- The effectiveness of the treatment selected shall be checked regularly against an appropriate parameter (e.g., quality-of-life questionnaire, severity score) (Level of recommendation: strong)
- All actions or interventions must adhere to the lowest invasiveness law. A practical method might, for example, combine an operation with tributary sclerosis to meet the goal of minimizing invasiveness (Level of recommendation: strong)
- **Conservative treatment** can be considered in all stages of the disease (Level of recommendation: weak)
- Any stage of chronic venous insufficiency and varicose veins can be treated with compression. It may be used independently or in conjunction with other techniques (Level of recommendation: weak)
- Selection of the appropriate materials should be guided not only by the indication but also by any comorbidity and the patient's wishes (Level of recommendation: moderate)
- All patients with venous symptoms (CEAP classes C1s–C6) shall receive **compression** treatment to relieve the symptoms (Level of recommendation: strong)
- Spider veins and reticular varices should be treated with **compression** after liquid sclerotherapy since it enhances clinical outcomes and lessens hyperpigmentation (Level of recommendation: moderate)
- **Compression** treatment shall be applied after foam sclerotherapy of varicose saphenous veins and tributaries (Level of recommendation: strong)
- **Initial postoperative/postinterventional compression** therapy should be used following an operation or endovenous thermal treatment of the superficial vein system (Level of recommendation: moderate)
- Patients in whom residual symptoms of chronic venous incompetence persist despite invasive treatment should receive continued **compression** treatment (Level of recommendation: moderate)

- To improve patient adherence, the **compression** treatment shall be applied using the lowest medically justifiable resting pressure (Level of recommendation: strong)
- All patients with **compression** treatment shall be recommended to apply skin care, however long the treatment period and whatever the treatment indication (Level of recommendation: strong)
- If it is impossible or considered undesirable to treat symptomatic varicose veins, or if a symptomatic venous picture persists even after invasive treatment, conservative treatment with effective venous drugs can be applied (Level of recommendation: weak)
- The patient should be informed that the clinical impact of a **plant-based drug's** complete effectiveness can typically only be evaluated after a period of 2-4 weeks of continuous treatment (Level of recommendation: moderate)
- Drugs shall not be used in patients who have a known hypersensitivity (allergy) to the drug in question (Level of recommendation: strong)
- The following negative effects need to be taken into consideration: Intestinal discomfort and skin reactions are the main side effects listed for oral administration of medication (standardized red vine leaf extract (AS 195), standardized horse chestnut extract, and oxerutin). If these side effects appear, switching to one of the other two vein medicines should be done (Level of recommendation: strong)
- If compression therapy, invasive varicose vein treatment, and medication therapy are unable to significantly reduce the venous oedema in a patient with varicose veins, **manual lymphatic drainage** may be attempted (Level of recommendation: weak)
- In treatment planning, it shall be considered that the incompetence of the tributary may resolve itself after removal of the saphenous vein (Level of recommendation: strong)
- In invasive procedures that require the use of a tumescent solution, the combined application of a local anesthetic can avoid a second anesthetic procedure (Level of recommendation: weak)
- The following **open surgical techniques** must be used, depending on the specific indication: vein removal techniques (such as crossectomy, stripping, and phlebectomy) and vein-conserving ideas (such as CHIVA, extraluminal valvuloplasty) (Level of recommendation: strong)
- The following indications for varicose vein operations shall be followed: saphenous varicose veins, accessory varicose veins or tributaries, recurrent

varicose veins, varicose veins with venous angiodysplasia, superficial vein thrombosis, variceal bleeding (Level of recommendation: strong)

- The following absolute **contraindications** shall be observed in open varicose vein operations: acute thrombosis of the deep leg vein/iliac vein, peripheral arterial occlusion disease from Fontaine stage III (except by special indication), known pregnancy, and moribund patient (Level of recommendation: strong)
- In cases of clinical/hemodynamic importance with an incompetent or obstructed deep vein system, the interruption of incompetent perforator veins can be considered (Level of recommendation: weak)
- Various methods can be used for **stripping** the diseased vein segment, e.g., conventional stripping, invaginated stripping, cryostripping, extraluminal stripping, phlebectomy (Level of recommendation: weak)
- In cases of isolated tributary reflux, **phlebectomy** can be used as the only method (Level of recommendation: weak)
- Special attention shall be paid to the following possible intraoperative complications in open operative treatment of varicose veins: bleeding, injury to large vessels, nerve damage (Level of recommendation: strong)
- Special attention shall be paid to the following possible **postoperative complications** in open operative treatment of varicose veins: secondary bleeding/hematoma, wound infection/healing disturbances, lymph vessel disturbances, superficial/deep leg vein thrombosis, lung embolism (Level of recommendation: strong)
- Varicose vein treatment by open operative procedures offers the possibility of good postoperative outcomes with a clear improvement in quality of life. After technically correct crossectomy of the GSV, very low recurrence rates in the SFJ are reported (Level of recommendation: moderate)
- The **open surgical** approach allows for the inclusion of a variety of precautions against recurrence in varicose vein surgery. These precautions include the use of duplex ultrasonography for preoperative mapping, nonabsorbable suture for ligating the SFJ, and methods for closing the saphenous opening and the free endothelium of the SFJ stump (Level of recommendation: weak)
- In the right patients, extraluminal valvuloplasty can be utilized as a technique to preserve the saphenous vein. Its goal is to restore valve functionality in the SFJ area. This may result in improved saphenous vein performance (Level of recommendation: weak)
- The CHIVA procedure can be used in all clinical stages of primary varicose veins. It is not recommended in cases of postphlebitic alterations to the

saphenous vein or reflux in very thin saphenous veins, as calibre reduction is not possible in these cases (Level of recommendation: weak)

- **Thromboembolic drug prophylaxis** is not indicated in principle; however, it may be applied depending on the individual risk profile and the characteristics of the intervention (extent, duration, etc.) (Level of recommendation: weak)
- Any varicose veins that appear in a previously treated region shall be considered **recurrent varicose veins**, independent of the type of previous treatment (Level of recommendation: strong)
- Indications for **EVTA** should be incompetent GSV, SSV, or anterior accessory saphenous vein (AASV). Incompetence of the posterior accessory saphenous vein (PASV), perforator veins, long varicose segments in cases of venous malformation, and varicose vein recurrence may also be indications (Level of recommendation: moderate)
- To avoid sensory nerve damage, it may be a good idea not to treat the SSV with thermal techniques below the mid-calf (Level of recommendation: weak)
- After **endovenous thermal ablation**, venous thromboembolism (VTE) prophylactic drugs should be administered in accordance with the thrombosis prophylaxis guidelines (Level of recommendation: moderate)
- The laser energy density (**LEED**) applied should be in the range of 60–100 J/cm of vein. The energy density should be adapted to the vein diameter (Level of recommendation: moderate)
- To reduce undesired side effects such as ecchymosis, postoperative pain, and paresthesia, modified probes, such as radial emission heads, and longer wavelengths should be preferred (Level of recommendation: moderate)
- **Sclerotherapy** can be used for all forms of varicose veins (Level of recommendation: weak)
- Absolute **contraindications** to sclerotherapy are known allergies to the sclerosant, acute venous thromboembolism, and local infection in the region to be treated or a severe generalized infection (Level of recommendation: strong)
- In patients with known **thrombophilia** and a high risk for thrombus formation, sclerotherapy should be carried out under additional prophylactic drugs to guard against thrombosis (Level of recommendation: moderate)
- In routine foam **sclerotherapy**, no more than 10ml of foam should be injected per day/ session. Larger volumes of foam may be injected after individual risk–benefit assessment (Level of recommendation: moderate)

- Mechanochemical endovenous ablation (**MOCA**) can be used as an alternative to other sclerotherapy methods for saphenous vein sclerotherapy (Level of recommendation: weak)

Varicose veins in pregnancy

- Invasive treatment of varicose veins during **pregnancy** should be indicated only in exceptional cases (Level of recommendation: moderate)

Figure 8 provides a comprehensive treatment algorithm for the management of patients with symptomatic CVD as per the S2k 2022 guidelines.

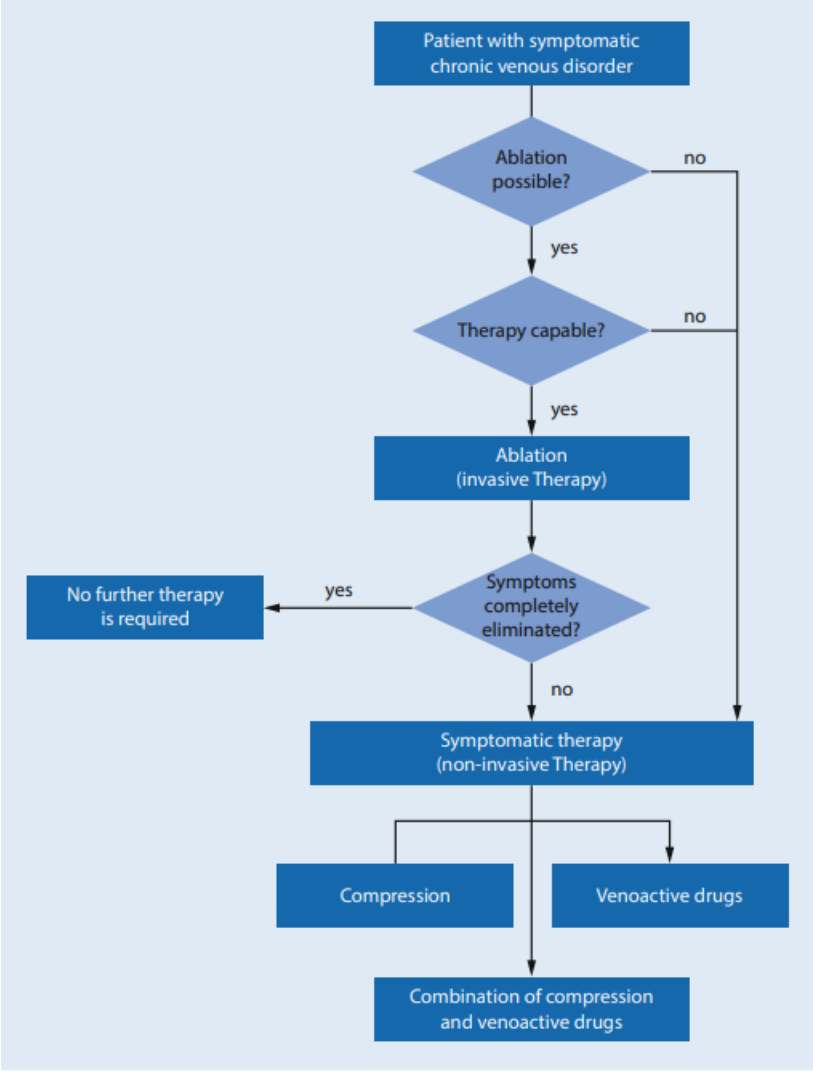


Figure 8. *Treatment or Combination of Treatments for Symptomatic Chronic Vein Disease (Retrieved from S2k 2022 Guidelines)*

1.3 International Guidelines

1.3.1 Australian Family Physician Recommendations (2013)

The Australian Family Physician recommendations drew focus on natural history, assessment, and management of varicose veins[13].

- Important changes have been adopted in the classification, scoring and anatomical notation of varicose veins in the past few years.
- A quality of life or degree of disability assessment is an important part of the initial consultation.
- Many patients simply require reassurance, and a thorough discussion of options at the primary care level may circumvent unnecessary referral.
- **Compression stockings** alone may be appropriate for patients who are too unfit for intervention or those who do not wish to have any form of surgical intervention.
- Many patients are treated for cosmetic concerns alone, so it is important to manage patients' expectations.
- Minimally invasive treatment options such as **injection sclerotherapy** and **endovenous modalities** are becoming increasingly popular and have shown equivalence in short term outcomes.
- **Conventional open surgery** has also improved, with better outcomes, smaller incisions and duplex mapping.
- Patients with complications of varicose veins (CEAP 3–6); and those with clinical evidence of chronic deep vein insufficiency, especially venous eczema or ulceration, require referral to a **vascular surgeon.**

Section 2.0 Drug Therapy

2.1 Capillary Stabilizing Agents

2.1.1 Aescin

Information on Aescin is detailed in the table below:

Table 14. Aescin Drug Information

SCIENTIFIC NAME **AESCIN (horse chestnut)**	
SFDA Classification[14]	Prescription
SFDA Approval	Yes
US FDA[15]	No
EMA[16]	Yes; March 2020
MHRA[17]	Yes
PMDA[18]	No
Indication (ICD-10)	I83
Drug Class	Capillary stabilizing agents
Drug Sub-class	Saponins
ATC Code	**C05CX03**
DRUG INFORMATION	
Dosage Form	Coated tablet
Route of Administration	Oral use
Dose (Adult) [DDD]*	**Horse chestnut extract (contains ≈20% aescin):** 300-600 mg by mouth daily for 8-12 weeks. **Aescin (20 mg/tab):** initial dose 40 mg three times per day, maintenance dose 20 mg/day
Maximum Daily Dose Adults*	**Horse chestnut extract (contains ≈20% aescin):** 600 mg. **Aescin (20 mg/tab):** 120 mg.
Adjustment	Renal impairment prior to treatment: - There is a concern that horse chestnut might make kidney disease worse. Do not use it in case

	of kidney problems Hepatic impairment prior to treatment: - There is one report of liver injury associated with using horse chestnut. If you have a liver condition, it is best to avoid horse chestnut.
Prescribing edits*	AGE
AGE (Age Edit): not indicated in children under the age of 7 years	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	- Most common: dizziness, headache, stomach upset, and itching - Most serious: muscle twitching, weakness, vomiting, diarrhea, depression, and paralysis.
Drug Interactions*	Moderate Interaction: - Medications that slow blood clotting (Anticoagulant / Antiplatelet drugs): Horse chestnut might slow blood clotting. Taking horse chestnut along with medications that also slow blood clotting might increase the risk of bruising and bleeding.
Special Population	Children: Use with caution
Pregnancy	- Taking the raw seed, bark, flower, or leaf is unsafe and can lead to death. There isn't enough reliable information to know if horse

	chestnut seed extract products are safe during pregnancy and breast-feeding, even if they have had the poisonous chemical esculin removed. Stay on the safe side and avoid use.
Lactation	- Taking the raw seed, bark, flower, or leaf is unsafe and can lead to death. There isn't enough reliable information to know if horse chestnut seed extract products are safe during pregnancy and breast-feeding, even if they have had the poisonous chemical esculin removed. Stay on the safe side and avoid use.
Contraindications	- Severe hypersensitivity
Monitoring Requirements	- Kidney function - hepatic function - signs and symptoms of bleeding
Precautions	- Kidney disease - Liver disease - Latex allergy - Surgery - Digestion problems - Bleeding disorders
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Varicose Veins treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for AESCIN.**

Table 15. Aescin HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Horse Chestnut (Aescin)	NICE	N/A
	CADTH	N/A
	HAS	N/A
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT – AESCIN

Aescin is recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention. No HTA analysis was conducted for Aescin by the concerned HTA bodies. Limitations for the use of Aescin include severe hypersensitivity.

2.1.2 Diosmin

Information on Diosmin is detailed in the table below:

Table 16. Diosmin Drug Information

SCIENTIFIC NAME DIOSMIN	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	No
EMA	Yes
MHRA	No
PMDA	No
Indication (ICD-10)	I83
Drug Class	Capillary Stabilizing Agents
Drug Sub-class	Bioflavonoids
ATC Code	**C05CA03**
DRUG INFORMATION	
Dosage Form	Film-coated tablet
Route of Administration	Oral use

Dose (Adult) [DDD]*	**600 mg/day in the morning before breakfast**
Maximum Daily Dose Adults*	3600 mg
Adjustment	Renal impairment prior to treatment: No dosage adjustment is recommended Hepatic impairment prior to treatment: No dosage adjustment is recommended
Prescribing edits*	AGE
AGE (Age Edit): The safety and efficacy of diosmin in children and adolescents aged less than 18 years have not yet been established.	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	- Most common: stomach pain, diarrhea, dizziness, headache, - Most serious: major skin redness and hives, muscle pain, blood problems, and altered heart rate.
Drug Interactions*	Moderate Interaction: Be cautious with this combination: - Chlorzoxazone - Diclofenac - Medications changed by the liver (Cytochrome P450 2C9 (CYP2C9) substrates) - Carbamazepine
Special Population	N/A
Pregnancy	Not enough is known about the use of diosmin during pregnancy and breast-feeding. Stay on the safe side and avoid use.

Lactation	Not enough is known about the use of diosmin during pregnancy and breast-feeding. Stay on the safe side and avoid use.
Contraindications	- Diarrhea - sarcoidosis - high calcium levels in the blood - kidney Stone - Addison's disease - high amount of potassium in the blood - Thomson disease
Monitoring Requirements	- Calcium level - Potassium level
Precautions	- Bleeding disorders: Diosmin might make bleeding disorders worse.
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Varicose Veins treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Diosmin.**

Table 17. Diosmin HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Diosmin	NICE	N/A
	CADTH	N/A
	HAS	N/A
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT – DIOSMIN

Diosmin is recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention. No HTA analysis was conducted for Diosmin by the concerned HTA bodies. Limitations for the use of Diosmin include sarcoidosis high calcium levels in the blood; kidney Stone; Addison's disease; high amount of potassium in the blood and Thomson disease.

2.1.3 Hesperidin/Diosmin

Information on Hesperidin/Diosmin is detailed in the table below:

Table 18. Hesperidin/Diosmin Drug Information

SCIENTIFIC NAME Hesperidin/Diosmin	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	No
EMA	No
MHRA	No
PMDA	No
Indication (ICD-10)	I83
Drug Class	Capillary Stabilizing Agents
Drug Sub-class	Bioflavonoids
ATC Code	**C05CA03**
DRUG INFORMATION	
Dosage Form	Film-coated tablet
Route of Administration	Oral use
Dose (Adult) [DDD]*	**In combination with diosmin (hesperidin 50 mg + diosmin 450 mg):** 2 tablets of daily in two divided doses, midday and evening at mealtimes for 6 months.
Maximum Daily Dose Adults*	400 mg hesperidin
Adjustment	Renal impairment prior to treatment: No dosage adjustment necessary. Hepatic impairment prior to treatment:

	No dosage adjustment required.
Prescribing edits*	AGE
AGE (Age Edit): The safety and efficacy of hesperidin in children and adolescents is not demonstrated. There are no studies available.	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	- Most common: stomach pain and upset, diarrhea, and headache. - Most serious: swelling of the mouth, face, and eyelids and the appearance of rashes
Drug Interactions*	Moderate Interaction; Be cautious with this combination: - Celiprolol - Diltiazem - Sedative medications (CNS depressants) - Verapamil
Special Population	N/A
Pregnancy	Hesperidin is POSSIBLY SAFE for pregnant or breast-feeding women when taken by mouth with diosmin.
Lactation	Hesperidin is POSSIBLY SAFE for pregnant or breast-feeding women when taken by mouth with diosmin.
Contraindications	- Severe hypersensitivity - History of bleeding or blood-clotting disorders
Monitoring Requirements	- CBC
Precautions	- Bleeding disorder: Hesperidin

	might slow blood clotting and increase the risk of bleeding. In theory, hesperidin might make bleeding disorders worse. - Low blood pressure: Hesperidin might lower blood pressure. In theory, taking hesperidin might make blood pressure become too low in people who already have low blood pressure. - Surgery: Hesperidin might prolong bleeding. There is concern that hesperidin might increase the risk of bleeding during and after surgical procedures. Stop taking hesperidin at least 2 weeks before a scheduled surgery.
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Varicose Veins treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Hesperidin.**

Table 19. Hesperidin HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Hesperidin	NICE	N/A
	CADTH	N/A
	HAS	N/A
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT – HESPERIDIN

Hesperidin is recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention. No HTA analysis was conducted for Hesperidin by the concerned HTA bodies. Limitations for the use of Hesperidin include severe hypersensitivity and a history of bleeding or blood-clotting disorders.

2.2 Peripheral Vasodilators

2.2.1 Pentoxifylline

Information on Pentoxifylline is detailed in the table below:

Table 20. Pentoxifylline Drug Information

SCIENTIFIC NAME PENTOXIFYLLINE	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	No
EMA	No
MHRA	Yes, data not available
PMDA	No
Indication (ICD-10)	I83
Drug Class	Peripheral Vasodilators
Drug Sub-class	Purine Derivatives
ATC Code	**C04AD03**
DRUG INFORMATION	
Dosage Form	Prolonged-release tablet
Route of Administration	Oral use
Dose (Adult) [DDD]*	**400 mg 3 times daily (with compression therapy)**
Maximum Daily Dose Adults*	1200 mg
Adjustment	Renal impairment prior to treatment: • CrCl ≥60 mL/minute: Oral: No dosage adjustment necessary. • CrCl 30 to <60 mL/minute: Oral: 400 mg twice daily

	• CrCl <30 mL/minute: Oral: 400 mg once daily Hepatic impairment prior to treatment: There are no dosage adjustments provided in the manufacturer's labeling. However, pentoxifylline exposure is increased with hepatic impairment; use with caution.
Prescribing edits*	N/A
AGE (Age Edit): N/A	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	- Most common: Nausea; vomiting - Most serious: Anaphylactic shock, anaphylactoid reaction, anaphylaxis, angioedema, angina pectoris, anorexia, anxiety, aplastic anemia, aseptic meningitis,
Drug Interactions*	- Ketorolac (Systemic): Risk X: Avoid combination - Vitamin K Antagonists (eg, warfarin): Risk C: Monitor therapy - Agents with Antiplatelet Properties (e.g., P2Y12 inhibitors, NSAIDs, SSRIs, etc.): Risk C: Monitor therapy
Special Population	Older adult: Use with caution in the elderly due to the potential for cardiac, hepatic, or renal impairment.
Pregnancy	Adverse events have been observed in animal reproduction studies.

Lactation	- Pentoxifylline and its metabolites are present in breast milk. - Due to the potential for serious adverse reactions in the breastfeeding infant, the manufacturer recommends a decision be made whether to discontinue breastfeeding or to discontinue the drug, considering the importance of treatment to the mother.
Contraindications	- Patients previously exhibiting intolerance to pentoxifylline, xanthines (eg, caffeine, theophylline), or any component of the formulation - Recent cerebral and/or retinal hemorrhage
Monitoring Requirements	- Renal function - Hemoglobin/hematocrit (especially in high-risk patients)
Precautions	- Anaphylaxis/anaphylactoid reactions - Hepatic impairment: Use with caution in patients with mild to moderate hepatic impairment - Renal impairment: Use with caution in patients with renal impairment
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Varicose Veins treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Pentoxifylline.**

Table 21. Pentoxifylline HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Pentoxifylline	NICE	N/A
	CADTH	N/A
	HAS [19]	It is possible to use 1,200 or 2,400 mg oral or intravenous pentoxifylline in addition to compression to treat venous ulcers (grade B). Level 2 trials show an increase in healing rates at 6 months. By extrapolation, the working group considered that pentoxifylline could also be used when compression is not possible. Pentoxifylline has not been granted a marketing authorization for venous ulcer treatment in France.
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT – PENTOXIFYLLINE

Pentoxifylline is recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention. According to HAS, it can be used in addition to compression to treat venous ulcers (grade B). Limitations for the use of Pentoxifylline include patients previously exhibiting intolerance to pentoxifylline, xanthines (eg, caffeine, theophylline), or any component of the formulation and those who had a recent cerebral and/or retinal hemorrhage.

2.3 Sclerosing Agents

2.3.1 Calcium Dobesilate Monohydrate

Information on Calcium Dobesilate is detailed in the table below:

Table 22. Calcium Dobesilate Monohydrate Drug Information

SCIENTIFIC NAME **CALCIUM DOBESILATE MONOHYDRATE**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	No
EMA	Yes; data not available
MHRA	No
PMDA	No
Indication (ICD-10)	I83
Drug Class	Antivaricose Therapy
Drug Sub-class	Sclerosing Agents
ATC Code	**C05BX01**
DRUG INFORMATION	
Dosage Form	Capsule
Route of Administration	Oral use
Dose (Adult) [DDD]*	**500 to 1000 mg/day**
Maximum Daily Dose Adults*	1000 mg
Adjustment	Renal impairment prior to treatment: No dosage adjustment necessary. Hepatic impairment prior to treatment: No dosage adjustment required.
Prescribing edits*	N/A
AGE (Age Edit): N/A	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions **(Most common and most serious)**	- Most common: Fever, gastrointestinal intolerance, skin reactions, and arthralgia

	- Most serious: throat tightness or swelling of the eyes, face, lips, or tongue, feel faint, or have difficulty breathing, agranulocytosis
Drug Interactions*	- Calcium dobesilate decreases the levels of Doxycycline. Separate intake by 2 hours. - Calcium dobesilate decreases the levels of Ofloxacin. Separate intake by 2 hours.
Special Population	N/A
Pregnancy	As it is not known whether calcium dobesilate crosses the placental barrier in humans, the drug should only be administered if the potential benefit justifies the potential risk to the fetus.
Lactation	This medicine is not recommended for use in breastfeeding women.
Contraindications	- Hypersensitivity to the active ingredient or to any of the inactive ingredients contained in the pharmaceutical formulation. - In women who are pregnant and breastfeeding.
Monitoring Requirements	- Kidney function and CBC prior to initiation
Precautions	- Renal impairment: Calcium Dobesilate should be used with caution in patients with a history of kidney disease and active kidney disease due to the increased risk of severe adverse effects. - Blood cell count: This medicine may lower the white blood cell count. Close monitoring of blood cell counts is necessary during treatment with this medicine. Do not start the treatment if the white blood cell count is low.
Black Box Warning	N/A

REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Varicose Veins treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Calcium Dobesilate.**

Table 23. Calcium Dobesilate HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Calcium Dobesilate	NICE	N/A
	CADTH	N/A
	HAS	N/A
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT – CALCIUM DOBESILATE

Calcium Dobesilate is recommended for the treatment of vein-related pain, leg heaviness, night cramps, and/or a sensation of swelling in symptomatic patients with varicose veins who are not candidates for intervention, who are waiting for intervention, or who have symptoms after intervention. No HTA analysis was conducted for Calcium Dobesilate by the concerned HTA bodies. Limitations for the use of Calcium Dobesilate include hypersensitivity to the active ingredient or to any of the inactive ingredients contained in the pharmaceutical formulation and pregnant and breastfeeding women.

Section 3.0 Key Recommendations Synthesis

IMAGING STUDIES

Imaging studies are generally not necessary for diagnosis, but they may be useful in patients with severe symptoms or in patients who are obese. They also may be helpful for planning procedures, documenting the extent of vascular pathology, or identifying the source of venous reflux.

Duplex Doppler ultrasonography is a simple, noninvasive, painless, readily available modality that can assess the anatomy and physiology of the lower extremity venous system. It can evaluate for acute and occult deep venous thrombosis, superficial thrombophlebitis, and reflux at the saphenofemoral and saphenopopliteal junctions. It can also assess the competence and diameter of the greater and lesser saphenous veins and the vascular architecture of the tributary and deeper perforating veins.

Other less commonly used studies that may be helpful in select patients include venography, light reflex rheography, ambulatory venous pressure measurements, photoplethysmography, air plethysmography, and foot volumetry.

CLASSIFICATION

Chronic venous disease is most commonly described using the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification system, with the clinical classification being as follows:

- C0: no visible or palpable signs of venous incompetence
- C1: spider veins and/or reticular varices
- C2: varicose veins
- C3: edema
- C4: changes to skin color and/or texture
- C5: cured or healed venous leg ulcer
- C6: active venous leg ulcer

TREATMENT

- **Conservative management**

Conservative treatment options include avoidance of prolonged standing and straining, elevation of the affected leg, exercise, external compression, loosening of restrictive clothing, medical therapy, modification of cardiovascular risk factors, reduction of peripheral edema, and weight loss.

External compression devices (e.g., bandages, support stockings, intermittent pneumatic compression devices) have been recommended as initial therapy for varicose veins; however, evidence to support these therapies is lacking.

Typical recommendations include wearing 20 to 30 mm Hg elastic compression stockings with a gradient of decreasing pressure from the distal to proximal extremity.

Multiple medications have been proposed as treatments for varicose veins. The use of diuretics is not supported by medical literature. Horse chestnut seed extract (Aesculus hippocastanum) has been used in Europe and has been shown in randomized, double-blind, placebo-controlled trials to reduce edema. Butcher's broom (Ruscus aculeatus) has also been used; however, clinical data to establish its safety and effectiveness are lacking.

- **External laser treatment**

Multiple laser machines that deliver various wavelengths of light through the skin and into the blood vessels are available to treat varicose veins. The light is absorbed in the vessels by hemoglobin, leading to thermocoagulation. Types of lasers include pulsed dye, long pulsed, variable pulsed, neodymium-doped yttrium aluminum garnet (Nd:YAG), and alexandrite lasers. Potentially, any small, straight vein branch is amendable to external laser ablation. However, laser therapy has typically been used on telangiectasias and smaller vessels rather than on larger veins. Long-pulsed lasers have been shown to completely clear veins with diameters less than 0.5 mm. For veins with diameters of 0.5 to 1.0 mm, improvement but not clearance is achieved.

- **Sclerotherapy**

Sclerotherapy involves injecting superficial veins with a substance that causes them to collapse permanently. A needle is inserted into the vein lumen and a sclerosing substance is injected. The substance displaces the blood and reacts with the vascular endothelium, sealing and scarring the vein. A variety of products are used, including hyperosmotic solutions (e.g., hypertonic saline), detergent solutions (e.g., sodium tetradecyl sulfate), and corrosive agents (e.g., glycerin). Injections typically work better on small (1 to 3 mm) and medium (3 to 5 mm) veins; however, a precise diameter used to make treatment decisions is lacking. Although sclerotherapy is a clinically effective and cost-effective treatment for smaller varicose veins, concerns about the development of deep venous thrombosis and visual disturbances, and the recurrence of varicosities have been noted.

- **Endovenous obliteration of the saphenous vein**

A newer treatment for varicose veins is to insert a long, thin catheter that emits energy (most commonly heat, radio waves, or laser energy). The released energy collapses and scleroses the vein. A variety of techniques and protocols are used. Because it is easier to insert a catheter through a vein in the same direction that the valves open, the catheter is most commonly inserted into a more distal portion of the vein and threaded proximally. Energy is released from the catheter tip. As the

catheter is pulled out, the vein lumen collapses. Bruising, tightness along the course of the treated vein, recanalization, and paresthesia are possible complications.

- **Surgery**

Historically, surgery is the best-known treatment for varicose veins, especially when the greater saphenous vein is involved. However, literature does not consistently support surgery as the definitive treatment option. Most surgical techniques involve using multiple smaller incisions to reduce scarring, blood loss, and complications.

Surgical management may reduce the risk of complications of varicose veins. Surgical correction of superficial venous reflux reduces 12-month ulcer recurrence. In addition, surgical management of venous ulcers leads to an 88 percent chance of ulcer healing, with only a 13 percent risk of ulcer recurrence over 10 months.

The simplest surgical procedure is ligation, which involves tying off the enlarged vein in portions of the leg, thigh, and groin. Potential complications include recurrence and worsening of intravenous pressure in tributary veins.

Phlebectomy and stripping are probably the best-known procedures; however, they are more of a collection of procedures than single techniques.

Typically, surgical procedures are done in a hospital operating room or in an out-patient surgical center. These procedures are associated with significant cost and risk of complications from anesthesia. Potential postsurgical complications include bleeding, bruising, and infection. In addition, a new blood vessel may form after the procedure, with the risk of neovascularization estimated to be as high as 15 to 30 percent.

- **Combination therapy**

Combinations of conservative measures and more invasive techniques may be appropriate, depending on the patient's symptoms, the extent of vascular pathology, and the available resources. For example, 12-month ulcer recurrence rates are significantly reduced in patients treated with compression and surgery compared with those treated with compression alone. A specific combination or standard protocol cannot currently be recommended.

- **Pregnancy**

Pregnant women presenting with varicose veins should be informed on the effects pf pregnancy on venous insufficiency. Interventional treatment should not be carried out unless in exceptional circumstances, and compression hosiery for symptom relief should be considered instead.

KEY RECOMMENDATIONS

- Conservative therapy (e.g., elevation, external compression devices, butcher's broom, horse chestnut seed extract, weight loss) for varicose veins may be helpful, but there are few clinical trials.
- There is insufficient evidence to preferentially recommend any specific treatment or combination of treatments for varicose veins.
- Sclerotherapy may be used to improve the symptoms and cosmetic

Section 4.0 Conclusion

The recommendations provided in this report are intended to assist in the management of Varicose Vein.

These recommendations should be used to support and not supplant decisions in individual patient management.

Section 5.0 References

1. Varicose Veins: Diagnosis and Treatment - PubMed. Accessed September 19, 2023. https://pubmed.ncbi.nlm.nih.gov/31150188/
2. Youn YJ, Lee J. Chronic venous insufficiency and varicose veins of the lower extremities. *Korean Journal of Internal Medicine*. 2019;34(2):269-283. doi:10.3904/kjim.2018.230
3. Busbaih Z, Saleh AAA, Alsulaiman AH, Almuhanna MA, AlKhawajah SH, Alsuwayie SB. Risk Assessment of Varicose Veins Among Teachers in Al-Ahsa, Saudi Arabia. *Cureus*. 2022;14(6). doi:10.7759/CUREUS.26125
4. Beebe-Dimmer JL, Pfeifer JR, Engle JS, Schottenfeld D. The epidemiology of chronic venous insufficiency and varicose veins. *Ann Epidemiol*. 2005;15(3):175-184. doi:10.1016/J.ANNEPIDEM.2004.05.015
5. Jones RH, Carek PJ. Management of varicose veins. *Am Fam Physician*. 2008;78(11):1289-1294.
6. Dalboh A, Alshehri NA, Alrafie AA, Bakri KA. Prevalence and awareness of varicose veins among teachers in Abha, Saudi Arabia. *J Family Med Prim Care*. 2020;9(9):4784. doi:10.4103/JFMPC.JFMPC_490_20
7. Heller JA, Evans NS. Varicose veins. *Vasc Med*. 2015;20(1):88-90. doi:10.1177/1358863X14566224
8. Gloviczki P, Lawrence PF, Wasan SM, et al. The 2022 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society clinical practice guidelines for the management of varicose veins of the lower extremities. Part I. Duplex Scanning and Treatment of Superficial Truncal Reflux: Endorsed by the Society for Vascular Medicine and the International Union of Phlebology. *J Vasc Surg Venous Lymphat Disord*. 2023;11(2):231-261.e6. doi:10.1016/J.JVSV.2022.09.004
9. Gloviczki P, Lawrence PF, Wasan SM, et al. The 2023 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society Clinical Practice Guidelines for the Management of Varicose Veins of the Lower Extremities. Part II. *J Vasc Surg Venous Lymphat Disord*. 2023;0(0). doi:10.1016/J.JVSV.2023.08.011
10. Overview | Varicose veins: diagnosis and management | Guidance | NICE. Accessed September 19, 2023. https://www.nice.org.uk/guidance/cg168
11. De Maeseneer MG, Kakkos SK, Aherne T, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2022 Clinical Practice Guidelines on the Management of Chronic Venous Disease of the Lower Limbs. *Eur J Vasc Endovasc Surg*. 2022;63(2):184-267. doi:10.1016/J.EJVS.2021.12.024

12. Pannier F, Noppeney T, Alm J, et al. S2k guidelines: diagnosis and treatment of varicose veins. *Hautarzt*. 2022;73(Suppl 1):1-44. doi:10.1007/S00105-022-04977-8

13. RACGP - Varicose veins – natural history, assessment and management. Accessed September 19, 2023. https://www.racgp.org.au/afp/2013/june/varicose-veins

14. Drugs List | Saudi Food and Drug Authority. Accessed September 19, 2023. https://www.sfda.gov.sa/en/drugs-list

15. U.S. Food and Drug Administration. Accessed September 6, 2023. https://www.fda.gov/

16. European Medicines Agency |. Accessed September 6, 2023. https://www.ema.europa.eu/en

17. MHRA Products | Home. Accessed September 6, 2023. https://products.mhra.gov.uk/

18. Pharmaceuticals and Medical Devices Agency. Accessed September 6, 2023. https://www.pmda.go.jp/english/

19. Haute Autorité de Santé - Managing venous leg ulcers (excluding dressings). Accessed September 19, 2023. https://www.has-sante.fr/jcms/c_459541/en/managing-venous-leg-ulcers-excluding-dressings

Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

Appendix B. Level of Evidence Description

ESVS guideline Level of evidence and Grade of Recommendations

Table 1. Levels of evidence according to ESC (European Society of Cardiology)

Level of evidence A	Data derived from multiple randomised clinical trials or meta-analyses
Level of evidence B	Data derived from a single randomised clinical trial or large non-randomised studies
Level of evidence C	Consensus of experts opinion and/or small studies, retrospective studies, and registries

Table 2. Classes of recommendations according to ESC (European Society of Cardiology)

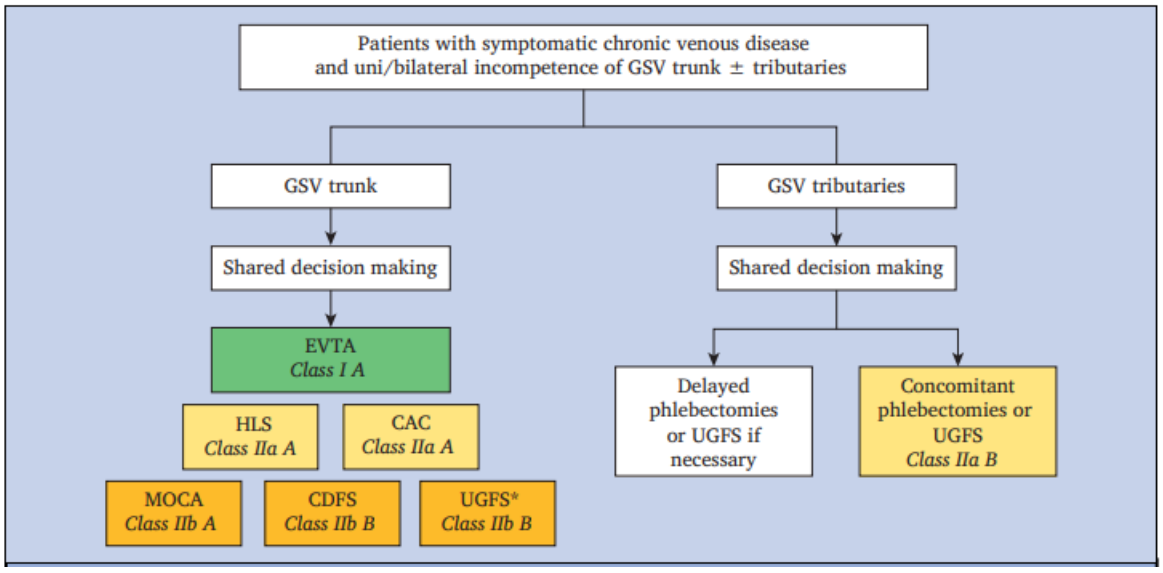
Class of recommendation	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful and effective
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy*
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion*
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful

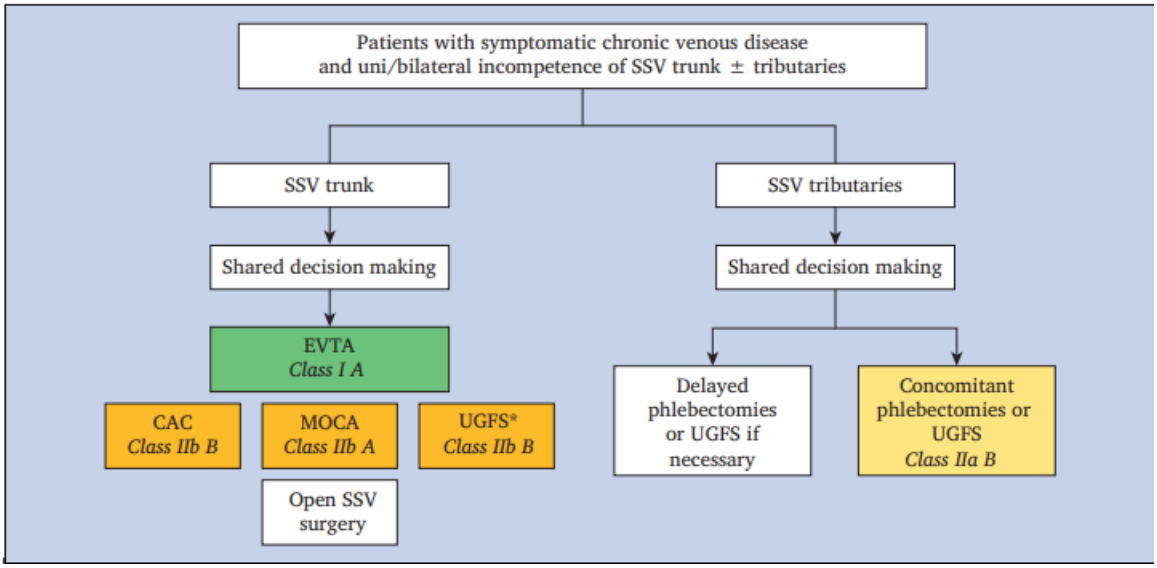
Appendix C. PubMed Search Methodology Terms

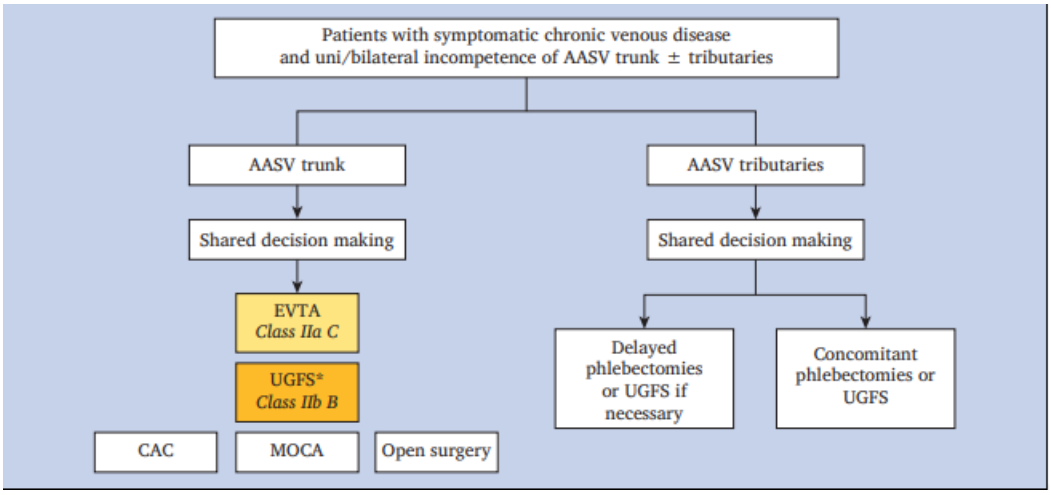
The following is the result of the PubMed search conducted for Varicose Veins guideline search:

Query	Sort By	Filters	Search Details	Results
(((((Varicose Vein Vein, Varicose Veins, Varicose Varix Varices) OR (Varicose Vein[Title/Abstract])) OR (Vein, Varicose[Title/Abstract])) OR (Veins, Varicose[Title/Abstract])) OR (Varix[Title/Abstract])) OR (Varices[Title/Abstract]) Filters: Guideline, in the last 5 years	Best Match	Guideline, in the last 5 years	((("varicose veins"[MeSH Terms] OR ("Varicose"[All Fields] AND "Veins"[All Fields]) OR "varicose veins"[All Fields] OR ("Varicose"[All Fields] AND "Vein"[All Fields]) OR "varicose vein"[All Fields]) AND ("varicose veins"[MeSH Terms] OR ("Varicose"[All Fields] AND "Veins"[All Fields]) OR "varicose veins"[All Fields] OR ("Vein"[All Fields] AND "Varicose"[All Fields]) OR "vein varicose"[All Fields]) AND ("varicose veins"[MeSH Terms] OR ("Varicose"[All Fields] AND "Veins"[All Fields]) OR "varicose veins"[All Fields] OR ("Veins"[All Fields] AND "Varicose"[All Fields]) OR "veins varicose"[All Fields]) AND ("varicose veins"[MeSH Terms] OR ("Varicose"[All Fields] AND "Veins"[All Fields]) OR "varicose veins"[All Fields] OR "Varix"[All Fields]) AND ("varice"[All Fields] OR "variceal"[All Fields] OR "varicose veins"[MeSH Terms] OR ("Varicose"[All Fields] AND "Veins"[All Fields]) OR "varicose veins"[All Fields] OR "Varices"[All Fields])) OR "varicose vein"[Title/Abstract] OR "vein varicose"[Title/Abstract] OR "veins varicose"[Title/Abstract] OR "Varix"[Title/Abstract] OR "Varices"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	15

Appendix D. ESVS Treatment Algorithm







Appendix E. S2k Treatment Algorithm