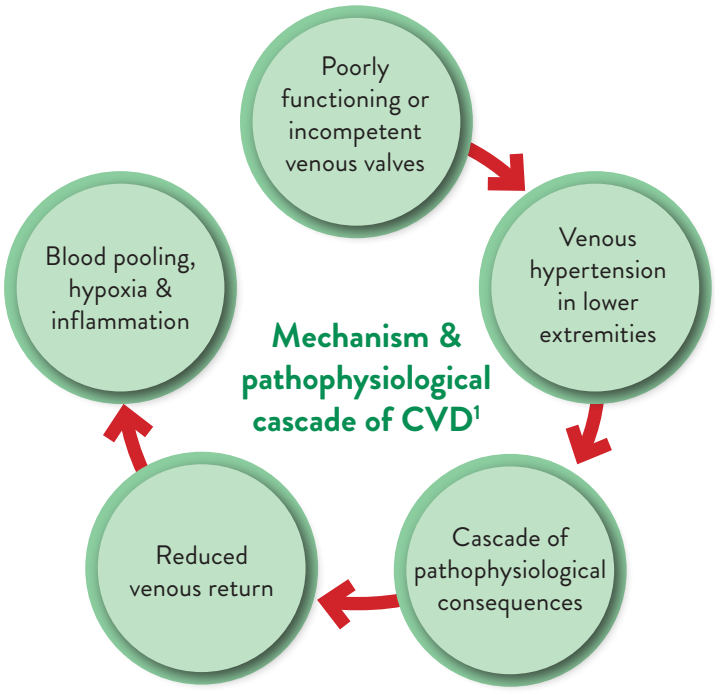
ISSUE 1

USE OF VENOACTIVE PRODUCTS IN CHRONIC VENOUS DISEASE

CHRONIC VENOUS DISEASE

- Chronic venous disease (CVD) is a common pathology, with significant physical and psychological impacts for patients.[1]
- Clinical spectrum of CVD - defined according to the CEAP (Clinical, Etiological, Anatomical, and Pathophysiological) classification - range from C0 to C6.
  - The term "chronic venous insufficiency" (CVI) is used when more advanced signs of CVD (C3–C6) are present.[1]



> **The term "chronic venous insufficiency" (CVI) is used when more advanced signs of CVD are present**

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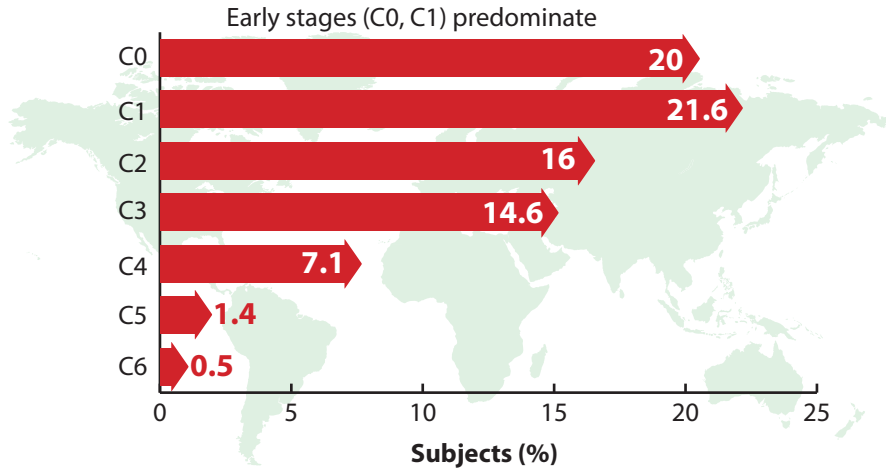
Venoruton oxerutin

GLOBAL PREVALENCE OF CVD

- Estimated prevalence of CVD in adults, typically diagnosed by the presence of varicose veins: **Between 5% and 65%** depending on the population.[1]
- The Vein Consult Program, an international, observational, prospective survey aiming to collect global epidemiological data on CVD also reported a higher worldwide prevalence of CVD (83.6%), thus showing that CVD affects a significant part of the global population.[2,3]

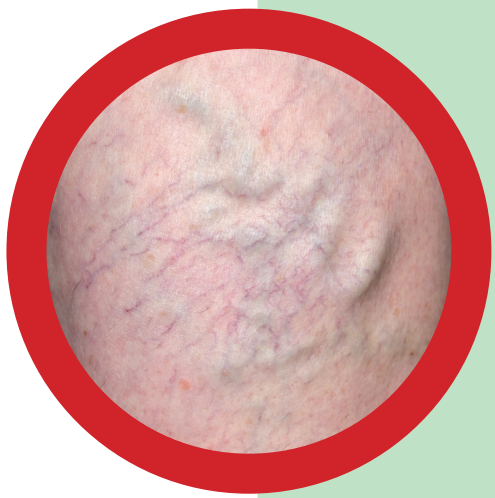
Prevalence of CVD (CEAP distribution as per the Vein Consult Program)[2,3]



Adapted from: Reference no. 2,3

> **CVD affects a significant part of the global population**

SIGNS & SYMPTOMS OF CVD



SIGNS

- Telangiectasia (spider veins)
- Varicose veins
- Edema or skin changes
  - » Eczema
  - » Hyperpigmentation
  - » Induration

SYMPTOMS

- Varying degrees of leg discomfort
  - » Pain
  - » Swelling
  - » Heaviness
  - » Cramps
  - » Burning

VENOACTIVE DRUGS IN THE MANAGEMENT OF CVD

Need of venoactives in CVD

1. Conservative treatment with compression stockings is generally the standard treatment option in patients presenting with varicose veins or early stage CVD to reduce symptoms and prevent disease progression.[1]

2. These compression stockings, although effective with general improvement of CVD, as well as ulcer healing, have poor treatment compliance that limits their effectiveness.[1]

3. Therefore, many CVD patients frequently require pharmacological treatment for CVD.[1]

4. Fortunately, venoactive drugs are available for use in these CVD patients, exerting significant beneficial effects on edema.[1]

5. In patients with CVI, hydroxyethylrutosides improve microvascular perfusion and microcirculation, reduce erythrocyte aggregation, and also exert a possible protective effect on the vascular endothelium.[4]

> **“Venoactive drugs are available for use in CVD patients, exerting significant beneficial effects on edema”**

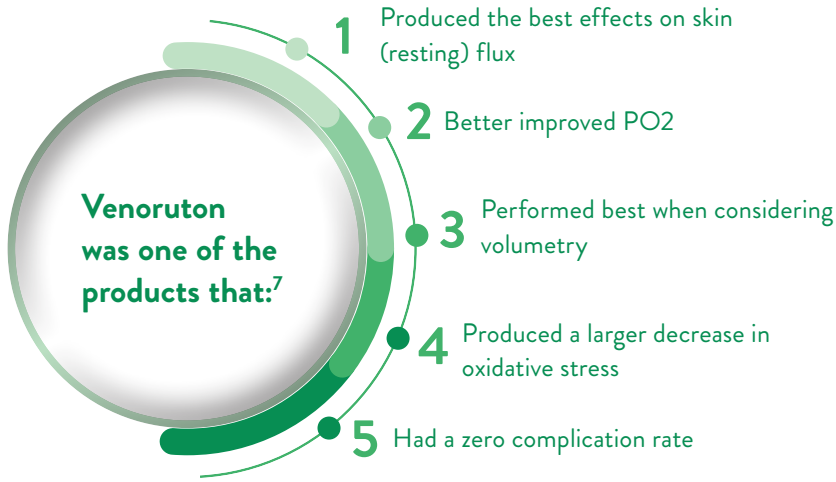
VENORUTON: ONE OF THE BEST OPTIONS IN CVI

- Venoruton has the potential to effectively improve the signs/symptoms of most patients with CVI.[5]
- Venoactive drugs provide symptom relief, improve quality of life, slow disease progression, and promote ulcer healing in patients with CVD.[6]

REGISTRY DATA ON THE EFFECT OF VENORUTON IN CVI

- A registry study aimed to compare several products used to control the symptoms of CVI, and found Venoruton among the best performers in comparison to Diosmin + hesperidin, Antistax, Escin and Elastic compression.[7]
- The dosages were used based on the locally approved practice in Italy.
- The registry included patients with CVI (CEAP grades 3–4a; and moderate to severe clinical symptoms).
- Main endpoints of the study were objective changes in microcirculation and limb volume (assessed by volumetry) and clinical CVI symptoms assessed on a visual analogue scale (VAS).

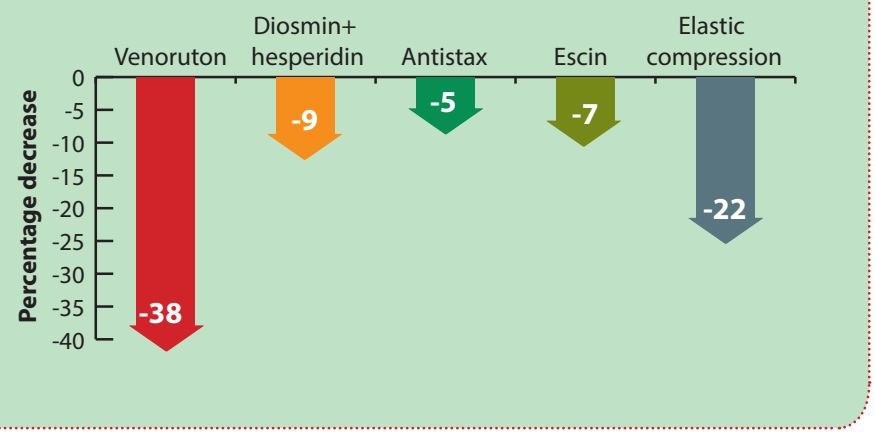
FINDINGS FROM THE REGISTRY[7]



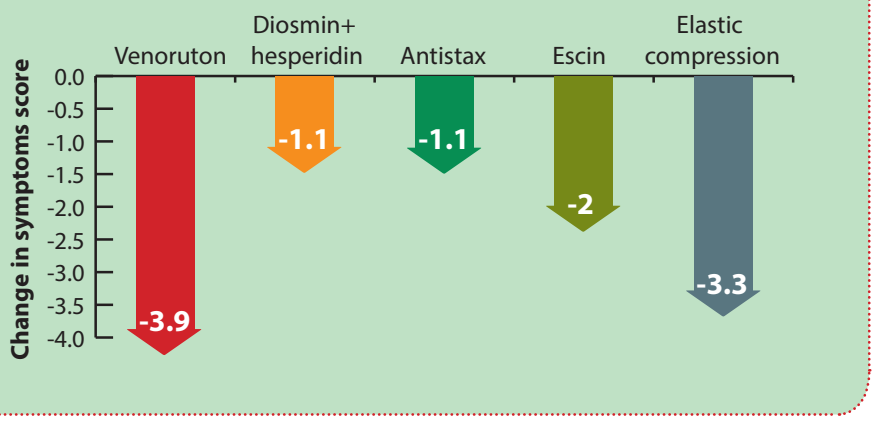
VENORUTON: A BETTER TREATMENT OPTION IN CVI[7]

> **Venoruton was one of the products that produced the best effects on skin (resting) flux**

Effect on resting flux

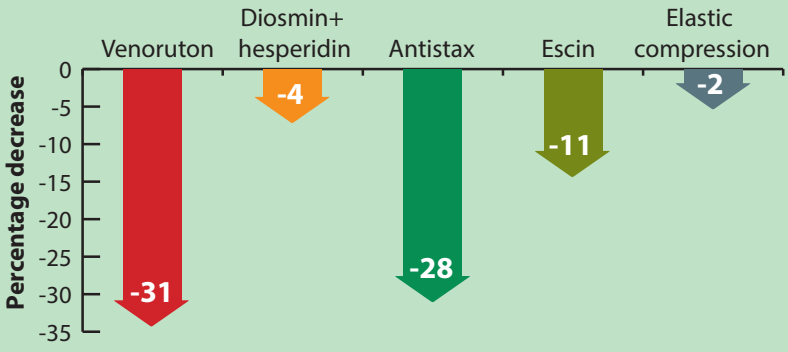


Symptoms scores

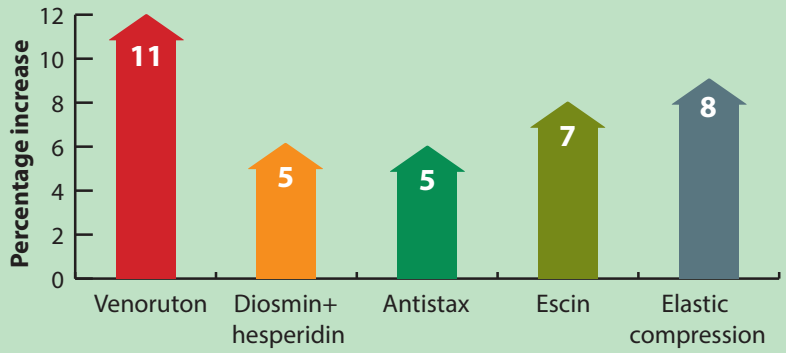


Adapted from: Reference no. 7

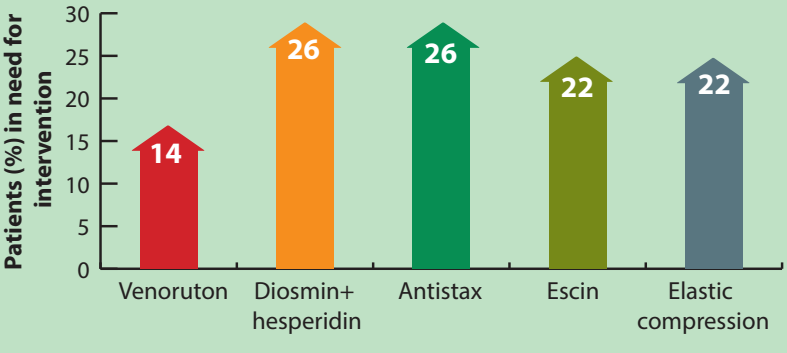
Oxidative stress



Transcutaneous PO2



Need for interventional treatments



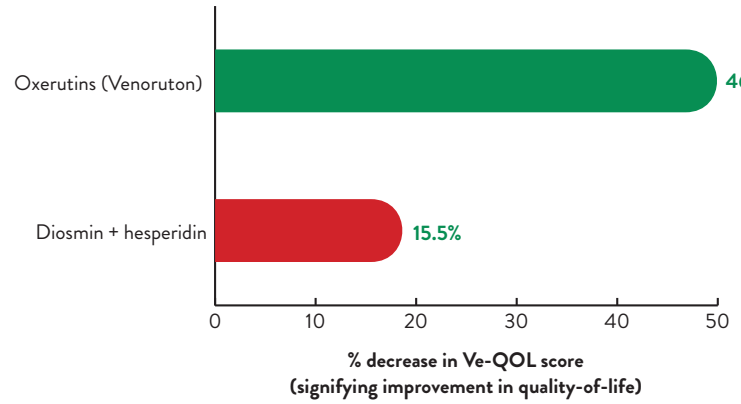
Adapted from: Reference no. 7

Venoruton was one of the products that produced a larger decrease in oxidative stress

VENORUTON: A BETTER VENOACTIVE THAN DIOSMIN

- Venoruton – a very safe and well-tolerated venoactive present in market for decades - is effective in controlling chronic venous hypertension, improves peripheral edema in CVI, and decreases the disease progression.[7,8]
- Importantly, venoruton appears to be more powerful and effective than the complex of diosmin + hesperidin (90% diosmin and 10% other flavonoids expressed as hesperidin) in CVI patients (considering edema, microcirculation, and the most common signs/symptoms).[7]
- An independent study investigating differences in efficacy between oxerutins (Venoruton; 2 g/day) and 500 mg micronized diosmin + hesperidin (D+H) in patients with CVI, evaluated venous-related quality-of-life (Ve-QOL).[5]
  - Results showed that there was a significant improvement in the oxerutins group (46.8% decrease in the Ve-QOL score; whereas change in Ve-QOL was significantly less in the D+H group (15.5%).

Changes in Ve-QOL score (signifying improvement in quality-of-life) in patients with CVI treated with oxerutins (Venoruton) vs. micronized diosmin + hesperidin



Ve-QOL – Venous-related quality-of-life

Adapted from: Reference no. 5

> **Venoruton appears to be more powerful and effective than the complex of diosmin + hesperidin in CVI patients**

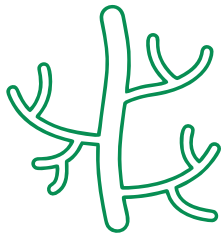
  - CVI, venous microangiopathy, and edema were significantly improved by the treatment with oxerutins; and the improvement in quality-of-life was significantly greater in the oxerutins group as compared with the D+H group.
  - In conclusion, treatment with oxerutins was comparatively more effective than micronized diosmin + hesperidin on the signs/symptoms of CVI and the quality-of-life of patients.[5]

EFFECTIVENESS OF VENOACTIVES IN PATIENTS WITH VARICOSE VEINS DURING PREGNANCY

- In short to medium term placebo-controlled studies (up to 6 months), hydroxyethylrutosides therapy improved signs and symptoms of CVI, including venous insufficiency associated with pregnancy, and was well tolerated.[4]
- A study evaluating the effectiveness of beta-hydroxyethylrutoside in patients with varicose veins in pregnancy found apparent beneficial clinical effects of the drug.[9]
  - In patients additionally given drugs, a significant reduction in leg circumference and diameter of vein (by sonography) was noted; leg circumference reduced by 3% and diameters of veins reduced by 15% on average.

Average reduction in leg circumference and diameters of varicose veins in pregnant women with varicose veins treated with beta-hydroxyethylrutoside

Leg circumference: reduced by **3%**



Diameters of veins: reduced by **15%**

Adapted from: Reference no. 9

› Oral hydroxyethylrutoside treatment during pregnancy may also associate with a fetal growth promotion effect as an added benefit.[10]

SOME OTHER TERMS COMMONLY USED IN REFERENCE OF VENORUTON

Hydroxyethylrutoside or O-(beta-hydroxyethyl)-rutoside

Rutin or oxerutin

Venoruton oxerutin

Has excellent safety profile and potential to effectively improve the signs/symptoms of most patients with CVI, with a zero complication rate[1,5,7]

Complications' (superficial venous thrombosis) rate with venoactives[7]				
Venoruton	Diosmin + hesperidin	Antistax	Escin	Elastic compression
0%	5.6%	5.5%	4.7%	3.4%

> **Hydroxyethylrutosides therapy improved signs and symptoms of CVI, including venous insufficiency associated with pregnancy**

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Venoruton
oxerutin

SACHETS

TABLETS

CAPSULES

EFFERVESCENT TABLETS

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