

# EVIDENCE BASED STATEMENT

DOMAIN **8**, Statement **6**

TOPIC: “**CALCIUM DOBESILATE EVIDENCE-BASED USE IN CHRONIC VENOUS DISEASE MANAGEMENT**”

## **SEARCH TERMS & SOURCES**

(calcium dobesilate) AND ((vein) OR (venous))  
PubMed, Embase and Cochrane Library

## **INCLUSION CRITERIA**

Indexed Journal, English Language, lower limb  
Reviews, <10 y.

## **SEARCH RESULT BEFORE - AFTER SELECTION**

20 (before) - 7 (after selection)

## **PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH**

1. Rabe E, Ballarini S, Lehr L, on behalf of the Doxium EDX09/01 Study Group. A randomized, double-blind, placebo-controlled, clinical study on the efficacy and safety of calcium dobesilate in the treatment of chronic venous insufficiency. *Phlebology*. 2016. 31(4) 264–274.
2. Orhurhu V, Chu R, Xie K, et al. Management of Lower Extremity Pain from Chronic Venous Insufficiency: A Comprehensive Review. *Cardiol Ther*. 2021 Jun;10(1):111-140
3. Alda O, Valero MS, Pereboom D. In vitro effect of calcium dobesilate on oxidative/inflammatory stress in human varicose veins. *Phlebology*. 2011;26(8):332–337
4. Mansilha A, Sousa J. Pathophysiological mechanisms of chronic venous disease and implications for venoactive drug therapy. *Int J Mol Sci*. 2018;19(6):1669.

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## Domain 8; Statement 6

### IDENTIFIED REFERENCES

- 1: Pompilio G, Nicolaides A, Kakkos SK, Integlia D. Systematic literature review and network Meta-analysis of sulodexide and other drugs in chronic venous disease. *Phlebology*. 2021 Oct;36(9):695-709.
- 2: Kitchens BP, Snyder RJ, Cuffy CA. A Literature Review of Pharmacological Agents to Improve Venous Leg Ulcer Healing. *Wounds*. 2020 Jul;32(7):195-207.
- 3: Martinez-Zapata MJ, Vernooij RW, Simancas-Racines D, et al. Phlebotonics for venous insufficiency. *Cochrane Database Syst Rev*. 2020 Nov 3;11(11):CD003229.
4. Martinez-Zapata MJ, Vernooij RW, Uriona Tuma SM, et al. Phlebotonics for venous insufficiency. *Cochrane Database Syst Rev*. 2016 Apr 6;4(4):CD003229.

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### TEXT FOR INCLUSION IN THE DOCUMENT

(300 words, not counting the references)

DOMAIN 8, Statement 6, TOPIC: “**CALCIUM DOBESILATE EVIDENCE-BASED USE IN CHRONIC VENOUS DISEASE MANAGEMENT**”

Calcium dobesilate (2,5-dihydroxy-benzenesulfonate) is a synthetic drug providing anti-inflammatory, anti-thrombotic and anti-oxidative effects. It reduces capillary hyperpermeability, It reduce blood viscosity and inhibits platelet aggregation. Laboratory data showed an increase in nitric oxide synthase and a decrease in prostaglandin release.

**[Alda O, Valero MS, Pereboom D. In vitro effect of calcium dobesilate on oxidative/inflammatory stress in human varicose veins. Phlebology. 2011;26(8):332–337]**

Clinically, it demonstrated a potential benefit in the control of edema, swelling, restless leg and pain in chronic venous disease (CVD) patients. Nevertheless, a recent randomized comparative trial showed no significant improvements compared to placebo in CVD related edema, symptoms, or quality of life.

**[Mansilha A, Sousa J. Pathophysiological mechanisms of chronic venous disease and implications for venoactive drug therapy. Int J Mol Sci. 2018;19(6):1669]**

A hypothesis has been made on a preferential role of Calcium dobesilate in the most advanced stages, but an evidence-based confirmation is still lacking.

**[Orhurhu V, Chu R, Xie K, et al. Management of Lower Extremity Pain from Chronic Venous Insufficiency: A Comprehensive Review. Cardiol Ther. 2021 Jun;10(1):111-140]**

Cases of transient agranulocytosis were reported following the use of calcium dobesilate, but a recent Cochrane revision did not identify a significant risk of it, showing just gastrointestinal events as possible side effects.

**[Kitchens BP, Snyder RJ, Cuffy CA. A Literature Review of Pharmacological Agents to Improve Venous Leg Ulcer Healing. Wounds. 2020 Jul;32(7):195-207].**

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## Domain 8; Statement 6

### STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 8, Statement 6

“Calcium Dobesilate demonstrated to potentially reduce venous incompetence related swelling, edema and pain, but more evidence is needed”

### 4 SELECTED REFEREENCES

1. Alda O, Valero MS, Pereboom D. In vitro effect of calcium dobesilate on oxidative/inflammatory stress in human varicose veins. *Phlebology*. 2011;26(8):332–337
2. Mansilha A, Sousa J. Pathophysiological mechanisms of chronic venous disease and implications for venoactive drug therapy. *Int J Mol Sci*. 2018;19(6):1669
3. Orhurhu V, Chu R, Xie K, et al. Management of Lower Extremity Pain from Chronic Venous Insufficiency: A Comprehensive Review. *Cardiol Ther*. 2021 Jun;10(1):111-140
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### identified LITERATURE BIAS

Heterogenous study populations

### SUGGESTED NEXT LINES OF RESEARCH

Head to head comparison with other venous active drugs  
Safety studies needed on the wide populations to estimate the risk of agranulocytosis