Varithena®
(polidocanol injectable foam) 1%

VANISH-1

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Investigator Group

Treatment of truncal incompetence and varicose veins with a single administration of a new polidocanol endovenous microfoam preparation improves symptoms and appearance

Study Design

VANISH-1 was a randomized, blinded, multicenter parallel group study designed to evaluate the efficacy and safety of 3 concentrations of polidocanol injectable foam, Varithena 0.5%, 1%, and 2%, compared with a placebo. A subtherapeutic dose of Varithena 0.125% was included as a control for blinding. The study population (n=279) consisted of patients who had saphenofemoral junction (SFJ) incompetence due to reflux of the great saphenous vein (GSV) or major accessory veins as determined by duplex ultrasound and superficial venous disease manifested by both symptoms and visible varicosities. The primary efficacy endpoint was patient-reported venous symptom improvement measured by change from baseline to Week 8 in 7-day average Varicose Veins Symptoms Questionnaire (VVSymQ®) score. Co-secondary efficacy endpoints assessed improvement in appearance of visible varicose veins from baseline to Week 8 as measured by scores of the Independent Photography Review–Visible Varicose Veins (IPR-V3) as well as the Patient Self-assessment of Visible Varicose Veins (PA-V3). The 3 tertiary endpoints were ultrasound response, change in Venous Clinical Severity Score (VCSS), and the modified Venous Insufficiency Epidemiological and Economic Study–Quality of Life/Symptoms (VEINES-QOL/Sym) score.

Polidocanol endovenous microfoam 1.0% is FDA approved as Varithena (polidocanol injectable foam).

Indications

Varithena (polidocanol injectable foam) is indicated for the treatment of incompetent great saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous vein (GSV) system above and below the knee. Varithena improves the symptoms of superficial venous incompetence and the appearance of visible varicosities.

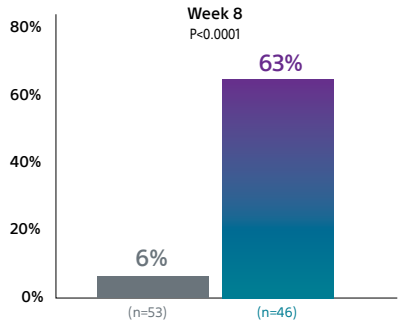
VANISH-1: Efficacy Results

• Clinically meaningful Improvement in varicose vein symptoms

Symptom improvement as measured by VVSymQ

- **VVSymQ electronic daily diary:** Patient-reported outcomes instrument developed in accordance with FDA guidance[1]
  - Patients rated daily duration of 5 symptoms: heaviness, achiness, swelling, throbbing, itching (HASTI™ symptoms)
  - VVSymQ score averages 7 daily scores (range 0 to 25)
- **Results:** At Week 8, VVSymQ scores for patients being treated with Varithena (polidocanol injectable foam) 1% had decreased significantly from baseline. In addition, scores for pooled Varithena patients were significantly superior to placebo (P<0.0001)

Percentage of Patients Reporting Clinically Meaningful Improvement

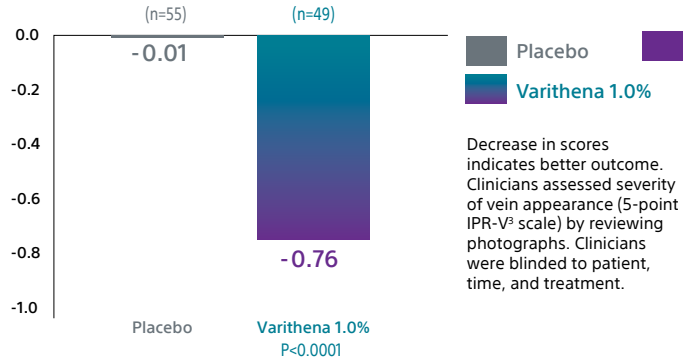


Clinically meaningful improvement =

"moderately improved" or "much improved" as reported on Patient Global Impression of Change (PGIC) scale

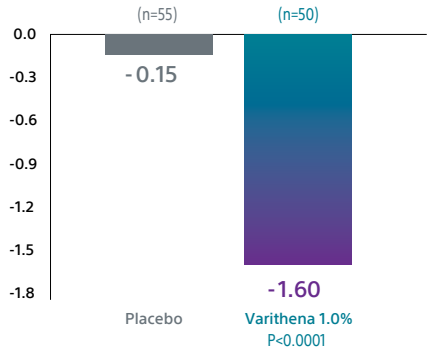
• Clinically meaningful improvement in appearance of varicose veins

- **Significantly Superior Results As Measured by IPR-V³:** Independent Photography Review–Visible Varicose Veins
  - Physicians rated appearance of patients' visible varicosities on a 5-point scale from baseline to Week 8



Decrease in scores indicates better outcome. Clinicians assessed severity of vein appearance (5-point IPR-V³ scale) by reviewing photographs. Clinicians were blinded to patient, time, and treatment.

- **Significantly Superior Results As Measured by PA-V³:** Patient Self-assessment of Visible Varicose Veins
  - Patients rated their varicose veins on a 5-point noticeability score at baseline, Week 4, and Week 8



Decrease in scores indicates better outcome. Using a 5-point noticeability score, each patient chose 1 of 5 statements that best described the actual appearance of visible varicose veins of the study leg. Measurements were taken at baseline, Week 4, and Week 8.

Notable Publications: Transient neurologic event following administration of foam sclerotherapy Phlebology. 2017 Feb;32(1):66-68 and Middle cerebral air embolism after foam sclerotherapy. Phlebology. 2012 27(8):430-3

VANISH-1: Efficacy Results (continued)

• Tertiary endpoints

Improvement as measured through duplex ultrasound response, VCSS, and VEINES-QOL/Sym

- **Duplex ultrasound response**
  - The duplex response rate for patients treated with Varithena (polidocanol injectable foam) 1% was 80.4%, demonstrating a significant superiority to the rate of those patients treated with Varithena 0.125%
- **VCSS and VEINES-QOL/Sym**
  - For patients treated with Varithena 1%, improvements in revised VCSS and VEINES-QOL/Sym scores at Week 8 were statistically superior to changes observed in the placebo group (P≤0.0001 in all cases)
  - Additionally, mean changes in revised VCSS and VEINES-QOL/Sym scores at Week 8 for patients in the pooled Varithena 0.5%, 1%, and 2% group were statistically superior to changes observed in the Varithena 0.125% group (P=0.0038 and P=0.0073)

VANISH-1: Safety Profile

In this trial, there were no serious adverse events (AEs) and no occurrences of pulmonary embolism (PE)

- In the 174 patients treated with any dose of Varithena that experienced AEs, 42% were mild while 18% were moderate. Severe AEs were seen in 12 patients.
  - **Most common AEs:** pain in extremity, superficial thrombophlebitis, infusion site thrombosis, injection site hematoma

VANISH-1: Conclusions

• Varithena:

- Demonstrated significant and clinically meaningful improvement in both the symptoms and the appearance of varicose veins in patients with an incompetent GSV and/or accessory saphenous veins and visible varicosities
- Is a minimally invasive, generally safe, non-surgical procedure
- Is associated with mostly mild or moderate adverse events with most resolved without sequelae
  - The most common adverse events observed were pain in extremity, superficial thrombophlebitis, infusion site thrombosis, and injection site hematoma

1. US Food and Drug Administration. Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Washington, DC: US Department of Health and Human Services; 2009.

Varithena (polidocanol injectable foam)
INDICATIONS Varithena (polidocanol injectable foam) is indicated for the treatment of incompetent great saphenous veins, accessory saphenous veins and visible varicosities of the great saphenous vein (GSV) system above and below the knee. Varithena improves the symptoms of superficial venous incompetence and the appearance of visible varicosities.

IMPORTANT SAFETY INFORMATION The use of Varithena is contraindicated in patients with known allergy to polidocanol and those with acute thromboembolic disease. Severe allergic reactions have been reported following administration of liquid polidocanol, including anaphylactic reactions, some of them fatal. Observe patients for at least 10 minutes following injection and be prepared to treat anaphylaxis appropriately. Intra-arterial injection or extravasation of polidocanol can cause severe necrosis, ischemia or gangrene. Patients with underlying arterial disease may be at increased risk for tissue ischemia. If intra- arterial injection of polidocanol occurs, consult a vascular surgeon immediately. Varithena can cause venous thrombosis. Follow administration instructions closely and monitor for signs of venous thrombosis after treatment. Patients with reduced mobility, history of deep vein thrombosis or pulmonary embolism, or recent (within 3 months) major surgery, prolonged hospitalization, or pregnancy are at increased risk for developing thrombosis. The most common adverse events observed were pain/discomfort in extremity, retained coagulum, injection site hematoma or pain, common femoral vein thrombus extension, superficial thrombophlebitis, and deep vein thrombosis. Physicians administering Varithena must be experienced with venous procedures, possess a detailed working knowledge of the use of the duplex ultrasound in venous disease and be trained in the administration of Varithena.

For Full Prescribing Information visit Varithena.com

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