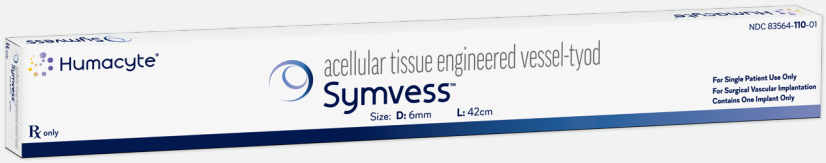
acellular tissue engineered vessel-tyod
Symvess™



Symvess™ Implantation Reference Guide

IMPORTANT NOTE This guide summarizes the Dosage and Administration section of the U.S. Prescribing Information for Symvess. It is not medical advice. Always consult the full U.S. Prescribing Information for the most accurate, up-to-date information regarding Symvess.

Recommended Supplies:[1]

- Symvess unit(s) (as needed)
- Sterile gloves
- Sterile surgical scissors
- Sterile scalpel blade (as needed)
- Sterile 750 mL or larger basin (as needed)
- Sterile atraumatic instruments
- 6mm Sheath tunneler (as needed)
- Sterile non-crushing vascular clamp
- 5-0 or 6-0 non-absorbable, monofilament suture
- Topical hemostatic agents (as needed)

DOSAGE[1]

Symvess is administered by surgical implantation to repair or replace the injured artery. The anatomical location in the extremity and length required should be determined by the surgeon implanting the graft based on the appropriate pre-operative clinical evaluation, vessel mapping and/or imaging, and intra-operative considerations. Symvess is provided as follows: 6mm in internal diameter and 42cm in length. Once removed from packaging, its usable length is approximately 40cm.

Each package (i.e., box containing Tyvek®‡ -sealed tray) contains one Symvess unit for administration to a single patient only.

Symvess may be trimmed to provide the length required for the artery replacement. Symvess can be trimmed to replace more than one injured extremity artery in the same patient.

INDICATION

SYMVESS is an acellular tissue engineered vessel indicated for use in adults as a vascular conduit for extremity arterial injury when urgent revascularization is needed to avoid imminent limb loss, and autologous vein graft is not feasible.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: GRAFT FAILURE

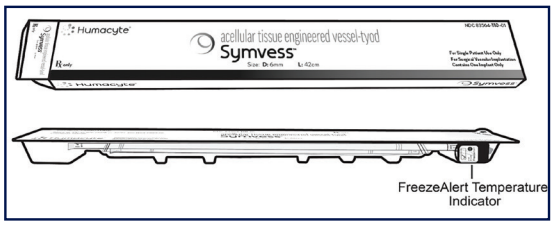
- Loss of SYMVESS integrity due to mid-graft rupture or anastomotic failure can result in life threatening hemorrhage.

PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.

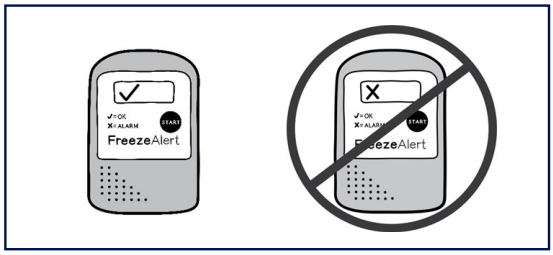
HANDLING STEPS[1]

Symvess is to be **handled** in an appropriate surgical environment as follows:

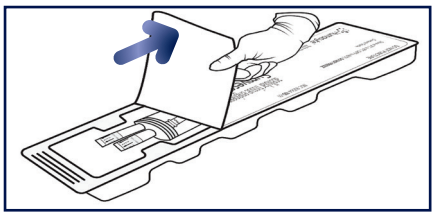
STEP 1: Symvess box contains a plastic thermoformed tray with a Tyvek®‡ lid. Open the box and remove the plastic tray.

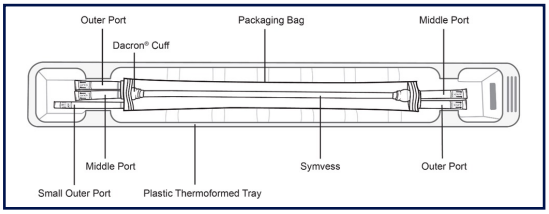


STEP 2: Confirm that the FreezeAlert™‡ indicator displays a check mark. ***If an "X" is displayed, Symvess has been exposed to freezing temperatures and should NOT be used - replace with a new Symvess.***



STEP 3: One sterile operator and one non-sterile operator are required to remove the sterile packaging bag containing Symvess from the plastic tray. Inspect the plastic tray to check for damage which can lead to loss in sterility of Symvess. ***Do not use if product is expired or has visible damage.*** If packaging is intact and within date of acceptable use, the non-sterile operator pulls back the Tyvek®‡ lid by the corner tab to open the plastic tray containing the sterile packaging bag, ***making sure to avoid touching the sterile contents inside the tray.***





IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

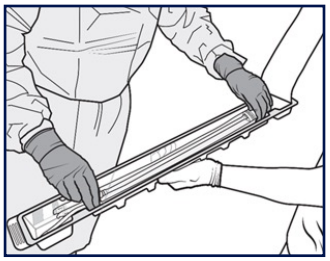
DO NOT use SYMVESS in patients who have a medical condition that would preclude long-term antiplatelet therapy (such as aspirin or clopidogrel) after resolution of acute injuries.

WARNINGS & PRECAUTIONS

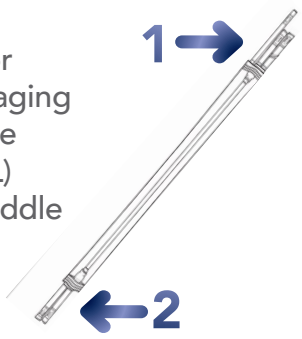
- **Graft Rupture:** Vascular graft rupture has occurred in patients treated with SYMVESS. Advise patients that arterial bleeding can be life-threatening and to seek emergent medical evaluation for any signs or symptoms of graft rupture such as bleeding, pain and swelling in the extremity, or signs of extremity ischemia. Follow appropriate procedures for handling and administering SYMVESS.

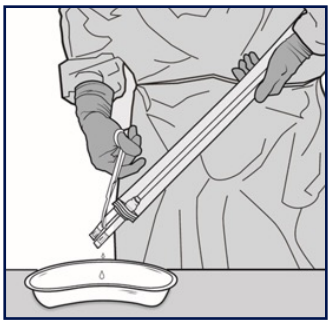
PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.

STEP 4: Non-sterile operator holds bottom of plastic tray with one hand and opens the Tyvek®‡ lid with the other. Sterile operator removes sterile bag from the tray grasping the ports (tubing) at the ends of the sterile packaging bag and places the sterile packaging bag on a sterile surface.

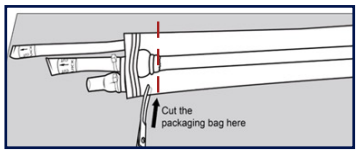


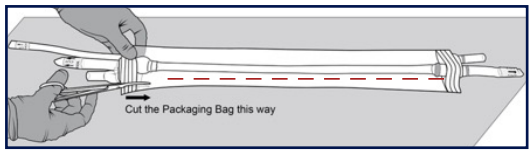
STEP 5: Symvess is suspended in sterile saline inside the packaging. Sterile operator cuts one or both of the outer ports on both ends of the packaging using sterile surgical scissors, and drains the sterile saline solution contained within the bag (~300 mL) into a sterile basin. Do not be concerned if the middle ports or the small outer port are accidentally cut.

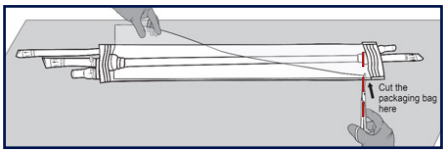




STEP 6: Place the drained packaging bag on a sterile surface. Using sterile surgical scissors or scalpel, sterile operator cuts a small slit on edge of packaging bag, makes a second cut along the length of the packaging bag. ***Be careful not to cut Symvess. If Symvess is accidentally nicked or cut during removal from the packaging bag, discard the damaged Symvess, and use a new one.*** Sterile operator makes another cut on the other end of the packaging bag to fully expose Symvess.





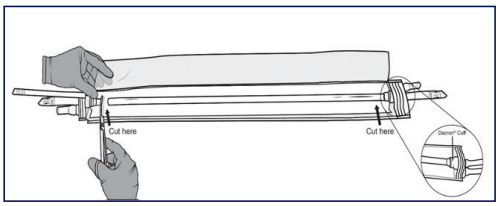


IMPORTANT SAFETY INFORMATION CONT'D

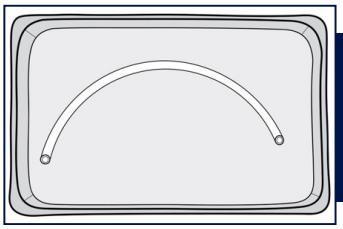
WARNINGS & PRECAUTIONS CONT'D

- **Anastomotic Failure:** Anastomotic failure has occurred in patients treated with SYMVESS. In clinical studies of SYMVESS, anastomotic failure occurred within the first 36 days post-implantation. Monitor patients for signs of anastomotic failure such as pain and swelling at the surgical site, decreasing hemoglobin or other signs and symptoms of bleeding. Advise patients to seek urgent medical evaluation if they have any signs or symptoms that may be indicative of anastomotic failure such as bleeding, swelling or worsening pain at the surgical site or changes in color of overlying skin. Follow appropriate procedures for handling and administering SYMVESS.

STEP 7: Holding back the flaps of the open packaging bag, sterile operator cuts Symvess 1cm from the Dacron®‡ cuffs (below blue sutures) to free it from the packaging bag. About 40cm in length of Symvess should be available for use.

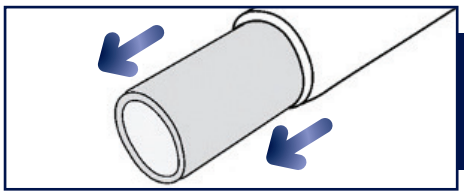


STEP 8: Use sterile gloves or ***atraumatic instruments*** to handle Symvess. Symvess is ready for immediate implantation OR keep it immersed in sterile saline solution (up to eight hours) while patient is being prepared.



IF SYMVESS DRIES OUT, IT IS NOT USABLE AND MUST BE DISCARDED

STEP 9: ***Symvess contains a clear silicone tube within the lumen*** to prevent Symvess from kinking and twisting when tunneling. ***The silicone tube can be left in place during any tunneling procedure. Before creating an anastomosis, remove the inner silicone tube*** by gently grasping the end of Symvess and sliding Symvess down to reveal the inner silicone tube, which can then be pulled out.



THE INNER SILICONE TUBE MUST BE REMOVED BEFORE CREATING AN ANASTOMOSIS

IMPORTANT SAFETY INFORMATION CONT'D

WARNINGS & PRECAUTIONS CONT'D

- **Thrombosis:** Thrombosis has occurred in patients treated with SYMVESS. In clinical trials of SYMVESS, patients received antiplatelet therapy following implantation of SYMVESS to reduce the risk of thrombosis. The risk of thrombosis may increase in patients who discontinue antiplatelet therapy. Anti-platelet therapy is recommended following treatment with SYMVESS.
- **Transmission of Infectious Diseases:** SYMVESS is manufactured using cells and reagents that may transmit infectious diseases or infectious agents. The cells used in the manufacture of SYMVESS are derived from a donor who met the donor eligibility requirements for transmissible infectious diseases. Animal-derived reagents are tested for animal viruses, bacteria, fungi, and mycoplasma before use, but this does not eliminate the risk of transmitting these or other transmissible infectious diseases and disease agents. No transmissible agent infections have been reported during clinical testing.

IMPLANTATION STEPS[1]

Symvess is **surgically implanted** under appropriate aseptic conditions by a trained surgeon.

- **STEP 1:** When handling Symvess, ***avoid using excessive force*** to prevent damage.
- **STEP 2:** To avoid damage or contamination, always use sterile gloves and ***atraumatic instruments*** when handling Symvess. Always protect Symvess from damage by heavy or sharp instruments.
- **STEP 3:** When necessary, a SHEATH TUNNELER may be used to safely deliver Symvess through subcutaneous or other tissues. Create a tissue tunnel that closely matches Symvess diameter (6 mm tunneller is recommended, but 8 mm tunneller is acceptable). ***A KELLY-WICK OR NON SHEATHED TUNNELLER IS NOT RECOMMENDED.*** During the tunneling process, ensure that Symvess does not kink or twist within the tunnel to prevent compromised flow and performance, thereby increasing the risk of thrombosis and failure.
- **STEP 4:** ***Keep the inner silicone tube in place within Symvess until any tunneling process is complete.*** Lubricate the tunneller sheath's lumen with saline solution and then gently push Symvess with the silicone tube through the sheath (alternatively Symvess can be grasped by or secured to the inner sheath rod and pulled through the sheath). After the tunneling sheath is removed, remove the inner silicone tube from Symvess.
- **STEP 5:** Following standard surgical procedures, the appropriate length to use for Symvess must be carefully determined. **SYMVESS DOES NOT ELONGATE UNDER PRESSURE**. The length must allow Symvess to adequately reach both anastomoses. Symvess should either be tunneled or held at the site of implantation so the length to adequately reach both anastomoses is clear. The patient's body size and posture, and the range of the motions likely to be encountered around the anatomical region of the implantation should be considered when determining length. Choosing the appropriate length may prevent kinking, twisting, or damaging Symvess after implantation.
- **STEP 6:** Failure to carefully cut Symvess may cause damage and result in failure at the anastomosis site or reduced suture retention strength. Cut Symvess with sharp vascular scissors as one would trim a human blood vessel prior to implantation. Symvess can be held with atraumatic instruments or sterile gloves while cutting with vascular scissors.

IMPORTANT SAFETY INFORMATION CONT'D

ADVERSE REACTIONS

The most common adverse reactions (≥3%) were thrombosis, fever, pain, anastomotic stenosis, rupture or anastomotic failure, and infection.

USE IN SPECIFIC POPULATIONS

Pediatric Use: The safety and effectiveness of SYMVESS in pediatric patients (0 to 17 years old) have not been established.

Geriatric Use: Two patients out of the 54 Extremity Group implanted with SYMVESS as a conduit in Study 1 were aged ≥65 years. The number of patients aged ≥65 years was not sufficient to determine whether they responded differently than younger patients to SYMVESS.

- **STEP 7:** ***The anastomosis must be precise, and with meticulous attention to detail.*** Symvess may be anastomosed end-to-end or end-to-side with the patient's vessels. An end-to-side anastomosis may accommodate size discrepancies between the host vessel and Symvess. Use of an appropriate anastomotic angle may minimize stresses upon Symvess which may reduce kinking and/or mechanical disruptions of Symvess, recipient or donor vessel, and/or suture lines.
- **STEP 8:** ***Use of non-crushing vascular (atraumatic) clamp is recommended*** on Symvess to avoid mechanical damage or disruption to Symvess. ***AVOID REPEATED, LOCALIZED CLAMPING OR EXCESSIVE CLAMPING ON ANY SYMVESS SECTION.***
- **STEP 9: Use only 5-0 or 6-0 non-absorbable, monofilament suture** with size selected based on the nature of the anastomosis. Use of a suture size larger in diameter than 5-0 or smaller in diameter than 6-0 for anastomosis creation with Symvess may reduce suture retention.
- **STEP 10:** ***A suture bite depth of 2.0-2.5mm*** is recommended to ensure suture retention.
- **STEP 11:** ***Flush static blood from the Symvess lumen while completing the second anastomosis***. Failure to do so may result in vessel thrombosis.
- **STEP 12:** Undue anastomotic bleeding may occur if gaps are present between Symvess and the host vessel. ***Use appropriate suture placement and avoid undue tension on the suture line***. At the surgeon's discretion, topical hemostatic agents may be used to minimize anastomotic bleeding if desired.
- **STEP 13:** Inspect the operative site carefully prior to closure. ***Ensure that Symvess is covered by muscle and/or soft tissue. Ensure that there are no twists, kinks, redundancy, before and during the tissue closure portion of the case***. It may be necessary to clear or release tissue to avoid Symvess impingement.
- **STEP 14:** At the conclusion of the operation, ***inspect the circulation to ensure that perfusion to the distal vascular bed has not been compromised and assess for risk of compartment syndrome following revascularization***.
- **STEP 15:** Surgical interventions are permissible and up to the surgeon's discretion. ***Symvess does not stretch. PERCUTANEOUS INTERVENTIONS SHOULD ONLY USE BALLOONS THAT DO NOT EXCEED 6MM IN DIAMETER***. Larger diameter balloons used for angioplasty or thrombectomy procedures may result in tearing of the Symvess wall or development of pseudoaneurysm. Mechanical thrombectomy devices other than balloons have not been studied with Symvess in the trauma setting and therefore are not recommended.

PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.

REFERENCE: 1. Symvess U.S. Prescribing Information. Durham, NC: Humacyte Global, Inc.

‡Indicates a third-party trademark.

For Symvess related questions, reach out to contactus@humacyte.com

Humacyte Global, Inc.
2525 E. Highway NC 54, Durham, NC 27713
www.symvess.com

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