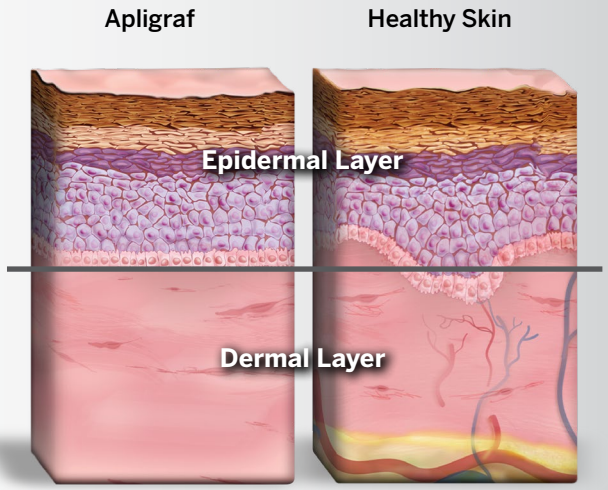
Apligraf® Has the Power To Transform the Wound Environment[1,2]

Description

- Apligraf is designed with living, bioactive cells to **LOOK**, **FUNCTION**, and **RESPOND** like human skin[3-5]
- The epidermal layer contains **LIVING KERATINOCYTES** and **STEM CELLS*** that provide potent healing signals (growth factors/cytokines)[3-6]
- The dermal layer contains **LIVING FIBROBLASTS** that proliferate and produce human collagen and other extracellular matrix (ECM) proteins as well as growth factors and cytokines[3-5]



* Stem cells are key contributors to Apligraf's signaling profile.[6]

Indications

- Apligraf is the **ONLY** product FDA-approved to heal venous leg ulcers (VLUs) after 4 weeks of failed conventional therapy[3]
- Apligraf is also FDA-approved to heal diabetic foot ulcers (DFUs) after 3 weeks of failed conventional therapy[3]

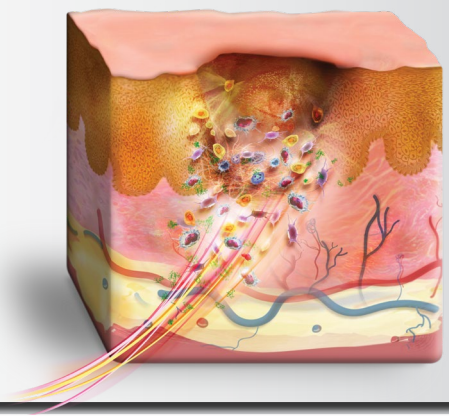
Cell Viability

- Apligraf cells are **BIOACTIVE** and poised to heal[4,7,8]
- Apligraf is delivered ready to use with **>90% CELL VIABILITY** throughout its 15-day shelf life[4]

Evidence of Mechanism of Action

- Apligraf transmits potent healing signals (growth factors/cytokines) that **CONVERT** the wound from a **CHRONIC** to an **ACUTE** state[1,2,7-9]
  - Keratinocytes activated at the wound edge
  - Growth factor signaling regulated and corrected
  - Inflammatory environment modulated
  - ECM production balanced

Patient's Cells Responsive After Apligraf



THE BIOTECH HEALER

Empowering you to optimize VLU outcomes

VLU = Venous Leg Ulcer

Organogenesis
Apligraf®
Living Cellular Skin Substitute

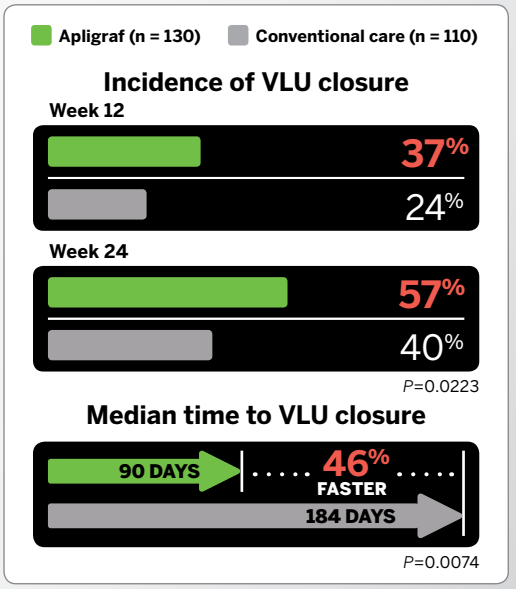
Apligraf Is the ONLY Product FDA-Approved to Heal VLUs

Apligraf Has Unsurpassed Proof in Healing VLUs[3,4]

- Apligraf's **EFFICACY** is **SUPPORTED** by a large, randomized controlled clinical (pivotal) trial (N=240) that was conducted under rigorous FDA review[3]
- The wounds studied in the pivotal trial were difficult to treat[4]
  - Greater than 50% of the wounds were present for more than 1 year
  - Wounds were large with a mean size of 14.2 cm^2
  - Greater than 50% of the wounds were full-thickness

Apligraf Closes More VLUs, Faster Than Conventional Therapy[3,4]

- **MORE PATIENTS** achieved **100% HEALING** with Apligraf plus conventional therapy versus conventional therapy alone[3,4]
- Apligraf-treated VLUs achieved healing **46% FASTER** than conventional therapy alone[3,4]



Apligraf Has Comprehensive Reimbursement Coverage*

Medicare Coverage[4]

- Apligraf is reimbursed by CMS as a skin substitute in the high bundle
- Apligraf is **COVERED** by **100%** of local coverage determinations (LCDs)

Unsurpassed Commercial Insurance Coverage[4]

- **ALL** commercial medical policies **COVER** Apligraf treatment
  - Supplied in 44 sq cm
  - Billed using HCPCS code Q4101 and CPT codes 15271-15278

*The coverage information provided is for educational purposes only and shall not be construed as a statement, promise, or guarantee that all information is accurate or reimbursement will be received. Reimbursement requirements are subject to change at any time, therefore, check with your local payer regularly.

For product information and technical, medical or reimbursement questions, please call 1-888-432-5232, OPTION 3.

Please refer to the Apligraf full prescribing information.

1. Stone RC, Stojadinovic O, Rosa AM, et al. A bioengineered living cell construct activates an acute wound healing response in venous leg ulcers. *Sci Transl Med*. 2017;9(371): eaa8611. doi:10.1126/scitranslmed.aaf8611. **2.** Stone RC, Stojadinovic O, Sawaya AP, Rosa AM, Badiavas E, Blumenberg M, Tomic-Canic M. Treatment of chronic venous leg ulcers with bioengineered living cell construct induces Metallothioneins and MMP8 to resolve matrix fibrosis and reactivates healthy remodeling response. Abstract presented at SAWC SPRING/WHS (2016). **3.** Apligraf [package insert]. Canton, MA: Organogenesis Inc.; 2017. **4.** Data on File, Organogenesis Inc. **5.** Schmid P. Immunohistologic characterization of Graftskin (Apligraf). *Wounds*. 2000;12(5 Suppl A):4A-11A. **6.** Carlson M, Faria K, Shamis Y, Leman J, Ronfard V, Garlick J. Epidermal stem cells are preserved during commercial-sale manufacture of a bilayered living cellular construct (Apligraf®). *Tissue Eng Part A*. 2011;17(3-4):487-493. **7.** Milstone LM, Asgari MM, Schwartz PM, Hardin-Young J. Growth factor expression, healing, and structural characteristics of Graftskin (Apligraf®). *Wounds*. 2000;12 (5 Suppl A):12A-19A. **8.** Falanga V, Isaacs C, Paquette D, et al. Wounding of bioengineered skin: cellular and molecular aspects after injury. *J Invest Dermatol*. 2002;119(3):653-660. **9.** Brem H, Young J, Tomic-Canic M, Isaacs C, Ehrlich HP. Clinical efficacy and mechanism of bilayered living human skin equivalent (HSE) in treatment of diabetic foot ulcers. *Surg Technol Int*. 2003;11:23-31.

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