



Apligraf®: The First Step Toward Healing

When conventional treatment is not leading to wound closure, Apligraf is a reliable, proven way to achieve more rapid and effective wound healing.^{1,2,3,4}

Apligraf is the only wound care product FDA-approved for healing both diabetic foot ulcers and venous leg ulcers. It's also the only therapy made from two types of living cells, which provide the wound with a healing supply of growth factors.

Only Apligraf is FDA-approved for the healing of both Venous Leg Ulcers and Diabetic Foot Ulcers.



VENOUS LEG ULCERS

Significantly more effective than compression therapy alone.

- **Improved Healing.** Apligraf achieved closure in more patients with venous leg ulcers >1 month's duration at 24 weeks than compression therapy (Unna's boot) alone (N=240, 57% vs 40%, $P=.022$).^{3,4}
- **Twice as effective with long-standing ulcers.** In patients with ulcers >1 year's duration (n=120), Apligraf plus compression therapy was more than twice as effective in achieving complete wound closure by week 24 (47% vs 19%, $P=.002$).^{3,4}
- **Effective alternative.** 74% complete wound closure in patients unresponsive to conventional therapy.⁵
- **More cost-effective.** Compared to the control, annual treatment cost was 27% lower with Apligraf (\$27,493 vs \$20,041).⁶

DIABETIC FOOT ULCERS

Significantly more effective than conventional therapy.

- **Improved Healing.** By 12 weeks of treatment, 56% (N=112) of ulcers treated with Apligraf plus conventional therapy were fully closed, compared to 39% (N=96) of ulcers treated with conventional therapy alone.⁷
- **Fewer amputations.** Apligraf-treated patients required significantly fewer amputations/resections of the study limb (6.3% vs 15.6%) [$P<.05$] compared to patients treated with conventional therapy at 6 months.⁷
- **Less Osteomyelitis.** Apligraf-treated patients had less incidence of Osteomyelitis at the Study Ulcer Site (2.7% vs 10.4%) [$P<.05$].⁷
- **More cost-effective.** Compared to the control, the Apligraf group had higher mean number of ulcer-free months (2.3 vs 1.5); was cost-effective based upon mean applications observed in routine clinical practice.⁸

For a clinical information package or to order, call 888-HEAL-2-DAY (888-432-5232) or visit apligraf.com

The persistence of Apligraf cells on the wound and the safety of this device in venous ulcer patients beyond 1 year and diabetic foot patients beyond 6 months have not been evaluated. Apligraf is indicated for use with standard therapeutic compression for the treatment of noninfected partial- and full-thickness skin ulcers due to venous insufficiency of duration greater than 1 month that have not adequately responded to conventional therapy. Apligraf is also indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than 3 weeks' duration that have not adequately responded to conventional ulcer therapy and that extend through the dermis, but without tendon, muscle capsule, or bone exposure. Apligraf should not be used on infected wounds or on patients with hypersensitivity to any components of Apligraf or the shipping medium. Please consult complete prescribing information for a description of epidermal and dermal elements contained in Apligraf. See Apligraf Essential Prescribing Information on reverse side. Apligraf is a registered trademark of Novartis Pharmaceuticals Inc. ©2007 Organogenesis, Inc.



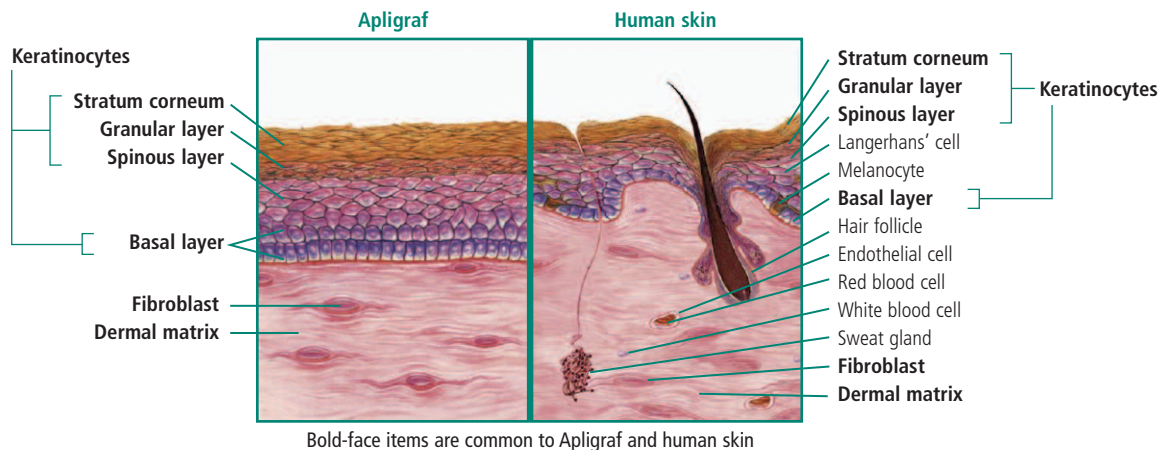
For product information,
please call:

888-HEAL-2-DAY
(888-432-5232)

Monday through Friday,
8:00 am to 5:00 pm EST

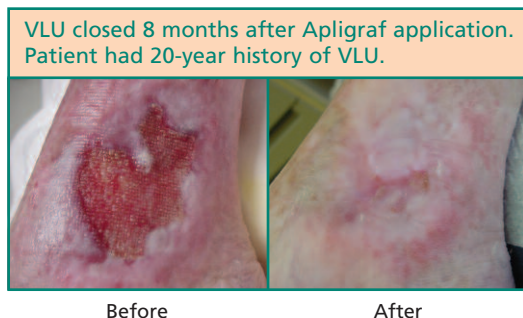
Or visit Apligraf.com

Approximates skin in structure and barrier function



- Consists of a living, active dermal layer composed of human fibroblasts derived from neonatal foreskin in a bovine type 1 collagen matrix and a living, active epidermal layer formed by human keratinocytes (with a well-differentiated stratum corneum)
- Contains matrix proteins, expresses cytokines and prevents desiccation
- Does not contain melanocytes, Langerhans' cells, macrophages or lymphocytes, or other structures such as blood vessels, hair follicles or sweat glands

Accelerates healing



Photos courtesy of Desmond P. Bell Jr, DPM



Photos courtesy of James R. De Meo, DPM

References: 1. Boulton AJM, Kirsner RS, Vileikyte L. Neuropathic diabetic foot ulcers. *N Engl J Med.* 2004;351:48-55. 2. Dove C, Sheehan P. An open-label, multicenter study evaluating the efficacy and safety of bilayered cell therapy in the treatment of diabetic foot ulcers. Hospital for Joint Diseases and NYU School of Medicine, New York, NY. Clinical Symposium on Advances in Skin and Wound Care, October 2005. 3. Falanga V, Sabolinski M. A bilayered living skin construct (Apligraf®) accelerates complete closure of hard-to-heal venous ulcers. *Wound Repair and Regeneration.* 1999;4:201-207. 4. Falanga V, Margolis D, et al., and the Human Skin Equivalent Investigators Group. Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. *Arch Dermatol.* 1998;134:293-300. 5. Brem H, Balledux J, Sukkarieh T, Carson P, Falanga V. Healing of venous ulcers of long duration with a bilayered living skin substitute: Results from a general surgery and dermatology department. *Dermatol Surg.* 2001;7:915-919. 6. Schonfeld WH, Villa KF, Fastenau JM, Mazonson PD, Falanga V. An Economic Assessment of Apligraf® for the Treatment of Hard-to-Heal Venous Leg Ulcers. *Wound Repair and Regeneration.* 2000;8:251-257. 7. Veves A, Falanga V, et al. Graftskin, a human skin equivalent, is effective in management of noninfected neuropathic diabetic foot ulcers. *Diabetes Care.* 2001;24:290-295. 8. Steinberg J, et al. A cost analysis of a living skin equivalent in the treatment of diabetic foot ulcers. *Wounds.* 2002;14(4):142-149.

(EPI) Apligraf® Essential Prescribing Information

Numbers in parentheses () refer to sections in the main part of the product labeling. **Device Description:** Apligraf is supplied as a living, bi-layered skin substitute manufactured using neonatal foreskin keratinocytes and fibroblasts with bovine Type I collagen. (1) **Intended Use/Indications:** Apligraf is indicated for use with standard therapeutic compression in the treatment of uninfected partial and/or full-thickness skin loss ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy. (2) Apligraf is indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness foot ulcers of neuropathic etiology of at least three weeks duration, which have not adequately responded to conventional ulcer therapy and extend through the dermis but without tendon, muscle, capsule or bone exposure. (2) **Contraindications:** Apligraf is contraindicated for use on clinically infected wounds and in patients with known allergies to bovine collagen or hypersensitivity to the components of the shipping medium. (3, 4, 5, 8) **Warnings and Precautions:** If the expiration date or product pH (6.8-7.7) is not within the acceptable range DO NOT OPEN AND DO NOT USE the product. A clinical determination of wound infection should be made based on all of the signs and symptoms of infection. (4, 5) **Adverse Events:** All reported adverse events, which occurred at an incidence of greater than 1% in the clinical studies are listed in Table 1, Table 2 and Table 3. These tables list adverse events both attributed and not attributed to treatment. (6) **Maintaining Device Effectiveness:** Apligraf has been processed under aseptic conditions and should be handled observing sterile technique. It should be kept in its tray on the medium in the sealed bag under controlled temperature 68°F-73°F (20°C-23°C) until ready for use. Apligraf should be placed on the wound bed within 15 minutes of opening the package. Handling before application to the wound site should be minimal. If there is any question that Apligraf may be contaminated or compromised, it should not be used. Apligraf should not be used beyond the listed expiration date. (9) **Use in Specific Populations:** The safety and effectiveness of Apligraf have not been established in pregnant women, acute wounds, burns and ulcers caused by pressure. **Patient Counseling Information:** VLU patients should be counseled regarding the importance of complying with compression therapy or other treatment, which may be prescribed in conjunction with Apligraf. DFU patients should be counseled that Apligraf is used in combination with good ulcer care including a non-weight bearing regimen and optimal metabolic control and nutrition. Once an ulcer has healed, ulcer prevention practices should be implemented including regular visits to appropriate medical providers. **Treatment of Diabetes:** Apligraf does not address the underlying pathophysiology of neuropathic diabetic foot ulcers. Management of the patient's diabetes should be according to standard medical practice. **How Supplied:** Apligraf is supplied sealed in a heavy gauge polyethylene bag with a 10% CO₂/air atmosphere and agarose nutrient medium, ready for single use. To maintain cell viability, Apligraf should be kept in the sealed bag at 68°F-73°F (20°C-23°C) until use. Apligraf is supplied as a circular disk approximately 75 mm in diameter and 0.75 mm thick. (8) **Patent Numbers:** 4,485,096; 5,106,949; 5,536,656. **Manufactured and distributed by:** Organogenesis Inc., Canton, MA 02021 REV: APRIL 2006

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