

# An Evaluation of Healing Metrics Associated with Commonly Used Advanced Wound Care Products for the Treatment of Chronic Diabetic Foot Ulcers



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## Background

- As rates of diabetes escalate worldwide, diabetic foot ulcers are an increasingly significant public health problem.
- Approximately one-quarter of people with diabetes will develop a foot ulcer over their lifetime.<sup>1</sup>
- Many diabetic foot ulcers will not heal with conventional therapy.
- The Wound Healing Society guidelines recommend consideration of advanced wound therapies if a diabetic ulcer does not reduce in size by 40% or more after 4 weeks of standard therapy.<sup>2</sup>
- Advanced wound therapies that promote rapid and complete healing, thus reducing the risk for infection and amputation, can substantially improve quality of life while decreasing financial burdens to the individual and health care system.
- Clinical trial results have shown that bioengineered skin substitutes, such as Apligraf®, Dermagraft®, and EpiFix® promote wound closure, resulting in more frequent and rapid healing of chronic diabetic foot ulcers when compared with standard therapy.<sup>3,4,5</sup>
- Comparative effectiveness research offers an opportunity for improved clinical outcomes and quality by providing more and better information on how products perform, which in turn may reduce health care costs.

## Purpose

Our purpose is to compare standardized healing metrics in patients with diabetic foot ulcers treated with 3 widely used advanced wound healing products.

### References

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## Methods

### Design

- Retrospective analysis of data collected and reported in published randomized controlled trials, physician product prescribing information, and pre-market approval summary documents from the US FDA.
- Rates of complete wound closure within 12 weeks, time to healing, number of graft applications to wound closure, durability of healed wounds, and safety were examined for patients with diabetic ulcers treated with Apligraf®, Dermagraft®, or EpiFix®.

### Included

- Included for analysis were only data from patients with type 1 or type 2 diabetes receiving active intervention (Apligraf®, Dermagraft®, or EpiFix®).
- The Apligraf® (n=112) and Dermagraft® (n=130) study groups were identified from peer-reviewed publications of pivotal clinical study data.<sup>3,4</sup>
- The EpiFix® group (n=64) consisted of pooled data from patients enrolled in 3 separate randomized controlled trials of EpiFix® for the management of lower-extremity ulcers.<sup>5,6,7</sup>

### Treatment

- Treatments consisted of Apligraf® (up to 5 weekly applications), Dermagraft® (up to 8 weekly applications), or EpiFix® (weekly or every two week applications) applied until wound closure or up to 12 weeks, whichever came first.
- In all studies standard principles of diabetic foot care were adhered to.

## Results

- Complete wound closure within 12 weeks of treatment initiation occurred in 56%, 30%, and 92% of Apligraf®-, Dermagraft®-, and EpiFix®-treated ulcers, respectively.
- EpiFix®-treated ulcers had the shortest time to healing (median 14 days) and least amount of graft material used (14 cm<sup>2</sup>) vs the comparative products.
- Rate of ulcer recurrence was 5.9% for Apligraf® (after 6 months), 18.8% for Dermagraft® (after 8 months), and 5.6% for EpiFix® (after 9-12 months).

## Results

Table 1. Product comparisons.

	Apligraf®	Dermagraft®	EpiFix®
Product description	Neonatal fibroblasts cultured in bovine collagen matrix overlaid with neonatal keratinocytes	Neonatal fibroblasts cultured in polyglactin mesh	Dehydrated human amnion/ chorion membrane allograft
Regulatory pathway	Premarket approval	Premarket approval	HCT/P; PHS Act Section 361
Graft sizes available	One 44 cm <sup>2</sup> disc	One 37.5 cm <sup>2</sup> sheet	Multiple sizes: 1.5 - 49 cm <sup>2</sup>
Cost per graft <sup>1</sup>	\$1,806.14	\$1,688.34	Various costs depending on graft size, starting at \$329.70 for 14 mm disc
Storage considerations	Consists of living cells that must be kept sealed in nutrient medium and 10% CO <sub>2</sub> /air atmosphere under controlled temperature 68°F - 73°F (20°C-23°C). Shelf life up to 15 days.	Must be stored continuously at minus 75°C ± 10°C. For continuous storage, transfer of Dermagraft® from shipping container into freezer must take ≤60 seconds to ensure cell viability. Frozen 6-month shelf life.	Sterilized tissue that may be stored at ambient conditions for up to 5 years.
Wound application instructions	Remove from liquid-filled pouch. Use within 15 minutes.	24-step application process including thawing.	Remove from dry pouch.

HCT/P = Human Cells, Tissue, and Cellular and Tissue-Based Product. PHS = Public Health Service.

<sup>1</sup> CMS Reimbursement Schedule at <http://www.cms.gov/apps/ama/license.asp?file=/hospitaloutpatientpps/downloads/October-2013-Web-Addendum-B.zip>. Accessed June 20, 2014.

Table 2. Wound area and healing metrics.<sup>3-8</sup>

	Apligraf® (n=112)	Dermagraft® (n=130)	EpiFix® (n=64)
Wound area (cm <sup>2</sup> )	2.97 ± 3.10	2.31	2.72 ± 2.6
Mean grafts received *	3.9	5.7	2.4
Complete wound closure within 12 weeks	56%	30%	92%
	63/112	39/130	59/64
Median days to closure	65 (7, 88) (n=63)	NR	14 (7, 77) (n=59)
Ulcer recurrence	5.9% <sup>1</sup>	18.8% <sup>2</sup>	5.6% <sup>3</sup>
Adverse events** (infection, cellulitis, osteomyelitis)	22.3%	19%	1.6%

Data reported as mean ± SD, percentage, or median (min, max) as indicated. <sup>1</sup>At 6 months. <sup>2</sup>At 8 months (32 weeks). <sup>3</sup>At 9-12 months.

\* To healing or to maximum allowed during 12-week study period. \*\* Of study wound.

## Conclusions

The differences observed in the published literature suggest that treatment with EpiFix® results in the most rapid improvement and resolution of diabetic foot ulcers.

Figure 1. Rates of complete healing at 6, 9, and 12 weeks for Apligraf®, Dermagraft®, and EpiFix® groups

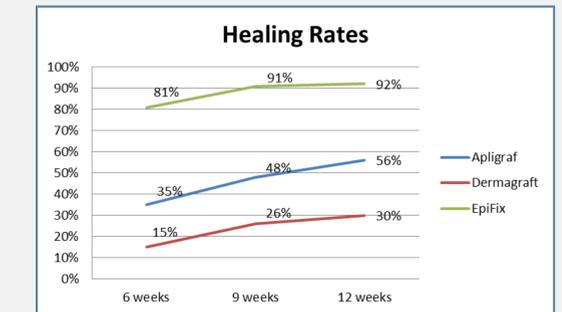
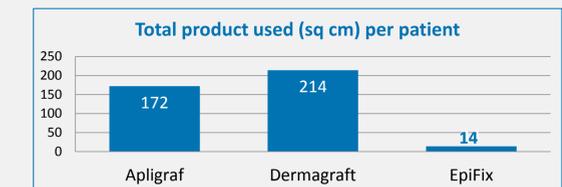
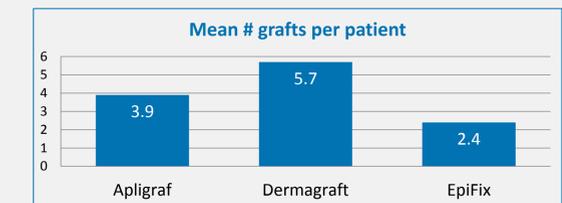


Figure 2. Comparison of quantity and estimated cost of products used per patient.



EpiFix® = PURION® Processed dehydrated human amnion/chorion membrane  
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Dermagraft® is a registered trademark of Organogenesis, Inc.  
Apligraf® is a registered trademark of Novartis