A Paper Supporting the CMS 2014 Hospital Outpatient Prospective Payment System Proposed Rule for Skin Substitutes

November 2013

Background

The Centers for Medicare and Medicaid Services (CMS) announced in July of this year that it was proposing changes to the way skin substitutes are reimbursed.

In the 2014 Hospital Outpatient Prospective Payment System (OPPS) proposed rule, which covers hospital outpatient and ambulatory surgery center reimbursements, CMS recommended packaging the products used in advanced wound care into one reimbursement payment. CMS noted that, in so doing, it was seeking to promote efficiency in the delivery of healthcare services and long-term cost containment.

The two largest suppliers in the skin substitute category, Shire (manufacturer of Dermagraft®) and Organogenesis (manufacturer of Apligraf®) began a vigorous lobbying effort against these proposed changes by CMS, claiming that there are "no other available products that are either interchangeable or comparable to the functionality or efficacy" of their therapies, and that such a move would result in patients "no longer having access to the treatment they get today". However, facts and the applicable data do not support such statements. Moreover, the data show the majority of wasted product in the skin substitute category stems from these two products.

Introduction

Currently, Medicare covers various skin substitutes, including products composed of materials ranging from synthetics to human or animal tissue.

Although skin substitutes are regulated differently by the FDA according to the characteristics of the product and the materials used, physician choice and reimbursement policies for procedures using skin substitutes are made based on the clinical function and efficacy of the product, NOT the regulatory pathway required to market the product. The regulatory pathway through which a product is reviewed by the FDA does not correlate to clinical effectiveness.

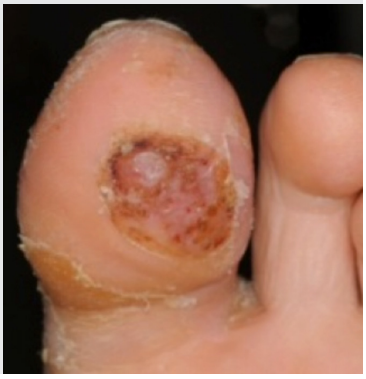
The purpose of this paper is to demonstrate that there are many products currently available in the market today that assist in the healing of chronic wounds, and some are more clinically effective and cost effective than the two products that have dominated the market and caused high levels of wastage for years. Accordingly, the efforts by CMS to change reimbursement in the skin substitute category will help to contain costs and will not negatively impact Medicare beneficiaries.

Chronic Wounds

Many patients suffer from different types of chronic wounds in the United States. The two single largest categories of chronic wound types are diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs).

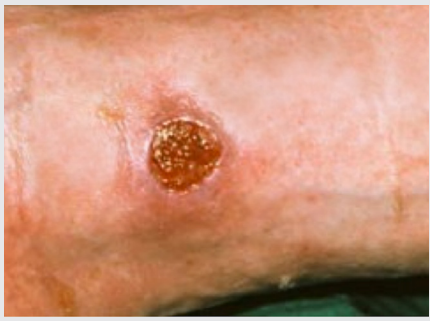
Diabetic Foot Ulcers (DFUs)

DFUs are wounds that develop on the feet of patients with Type I and Type II diabetes. They can be located anywhere on the foot and typically start from a trauma or continued pressure in a single area over time. When patients with diabetes lose the feeling in their feet, the opportunity for these small wounds to become large and/or infected is amplified. It is estimated there are 1,000,000[1] patients suffering from DFUs in the United States with a median area[2] of 1.35 square cm. For reference, the area of a U.S. dime is 2.52 square cm and a US quarter is 4.6 square cm. These DFUs can and often lead to amputation and/or death. In fact, diabetic patients with an amputation and an open ulcer are more likely to die within five years than patients suffering from prostate, breast and colon cancer combined[3].



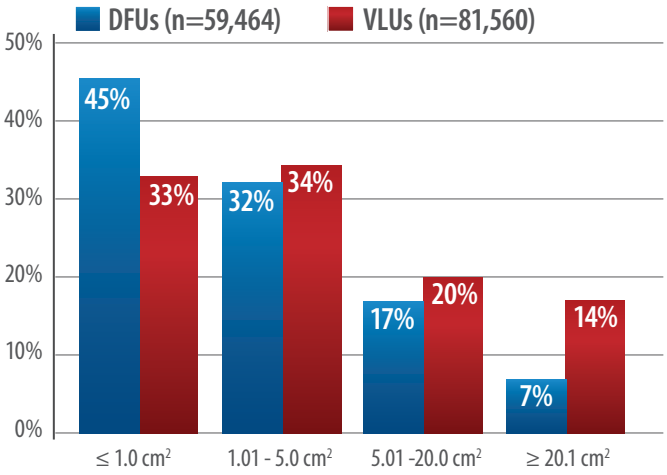
Venous Leg Ulcers (VLUs)

VLUs are wounds that develop in the lower leg of patients with venous insufficiency. Venous insufficiency occurs when the vein in the leg loses its efficiency in moving blood back up the leg to the heart. This results in the pooling of fluid in the lower leg, which contributes to over-saturation of the lower leg tissue and causes skin breakdown that ultimately turns into an open wound. There are approximately 860,000[1] VLUs in the U.S., with a median area[2] of 2.32 square cm. If VLUs are not healed, these ulcers can continue to enlarge to the point the open wound engulfs the entire lower leg. Many of these wounds are open for many months, if not years.



The majority of DFUs and VLUs are relatively small in size. The following charts[2] show that 77% of all DFUs and 67% of all VLUs have an area of less than 5.0 square cm. In addition, it shows that 93% of all DFUs and 86% of all VLUs have an area of less than 20.0 square cm.

Percent of DFUs and VLUs by Area (cm²)



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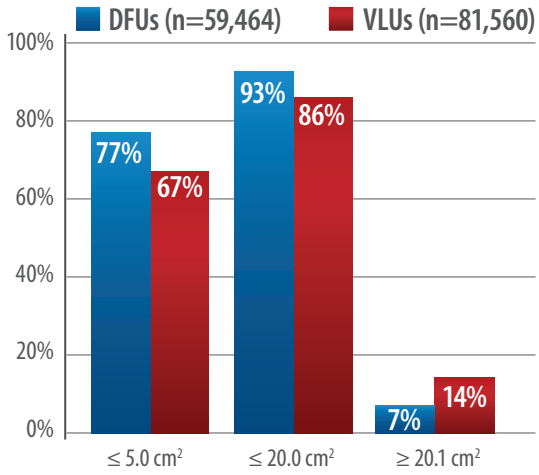


Nevertheless, Shire and Organogenesis, the two largest suppliers of skin substitutes for treatment of DFUs and VLUs, each produce only one graft size, each of which is significantly larger than the median size of a DFU or VLU. Dermagraft®, which is used to treat DFUs, comes in a sheet that is 37.5 square cm. Apligraf®, which is used to treat DFUs and VLUs, comes in a sheet that is 44 square cm. Because these are both single-use products, a treating physician who uses only 1.35 square cm of a 37.5 square cm sheet of a graft must discard in excess of 90% of the product. When a large portion of product is discarded, Medicare dollars are paying for product that is mostly wasted. Thus, a significant wastage problem exists with the current skin substitute reimbursement system and the two largest volume suppliers.

Data Analysis

Method: MiMedx retained a well-known independent third-party data aggregator[4] to perform data analyses for the Hospital Outpatient Prospective Payment System (OPPS) data file, which contains Medicare claims data from dates of service of January 1, 2011 through December 31, 2011. The analysis of skin substitutes includes data elements such as diagnosis codes and modifiers, as well as payment and charge amounts. From the reported charges, hospitals' outpatient costs can be derived using their cost-to-charge ratios. In total, the file includes data from 158,082 paid OPPS claims. This data does not include payments for doctors' office claims.

CMS has established specific billing codes for skin substitute products for the treatment of patients with chronic wounds. These billing codes are referred to as "Q Codes." In 2011 there were nineteen (19) Q Code products available to physicians to treat their Medicare patients, with 92% of the CMS reimbursement attributed to two products (Q4101, Apligraf®, and Q4106, Dermagraft®).

The analysis included a review of the data by Ambulatory Payment Classifications (APCs), including the DFU and VLU diagnoses, as well as the top two claim volume products (Q4101 and Q4106), by both product and diagnoses. From the qualifying claims in each group, cost, charge, and payment data were abstracted for only the applicable line items (i.e., not the total claim charge, cost, and payment amounts) so the differences among the various groups could be further analyzed. (See Table A).

CMS Claims Data Findings: There is a wide variation in the average payment amongst all of the analyzed Q codes, and there were a minimal number of claims for a number of the Q codes, as many of these products had only recently launched. MiMedx's EpiFix® (Q4131) product, for example, is not listed because the Q code was effective January 1, 2013.

TABLE A Comparison of Diabetic Foot Ulcer and Venous Leg Ulcer Groups with Q4101 and Q4106 Reported on Claim

	DFUs			VLUs		
Group	**APC 0134**	**APC 0135**	**APC 0136**	**APC 0134**	**APC 0135**	**APC 0136**
Claim Count	26,232	1,449	43	15,052	514	15
Average Charge	$8,052	$8,754	$6,050	$7,901	$7,513	$6,505
Average Cost	$2,073	$2,162	$1,322	$2,076	$1,929	$1,429
Average Payment	$2,413	$2,437	$2,499	$2,281	$2,204	$2,748

The data analysis also indicated the top two claim volume Q codes, Q4101 (Apligraf®) and Q4106 (Dermagraft®), represented $94M of the $101M paid in 2011. Under the current CMS system, skin substitutes are reimbursed on a per square centimeter basis. The relevant measurement is not the wound size, but rather the size of the product used to treat the wound. As noted above, if the median size of a DFU is 1.35 square cm and the size of the Dermagraft® and Apligraf® grafts are 37.5 square cm and 44 square cm respectively, one can conclude that for at least half of these grafts, over 90% of the product is wasted. This translates into wastage of over $91 million taxpayer dollars for CMS reimbursements in the hospital outpatient skin substitute category in CY2011.

Proposed CMS Reimbursement Changes and Impact on Chronic Wound Care

Multiple Effective Therapies are Available for Chronic Wounds: When Apligraf® and Dermagraft® first came to market over a decade ago, there were very few treatments available for chronic wound care. In recent years there have been significant advancements in this area, however, such that there are now thirty-six (36) products with Q codes that are available for chronic wound care under the skin substitute category. Many can be used to treat multiple types of chronic wounds – not just DFUs and VLUs; many have a record of better clinical effectiveness than the older therapies in terms of the number of applications needed and/or the number of days to heal a wound; and many offer a lower cost structure than the older therapies.

The newer products are not just "simple bandages"; instead, these therapies range from allograft tissues made from amniotic membranes to collagen matrices and xenografts. These products came to market through 510(k) or human cells, tissues, and cellular and tissue-based product (HCT/P) pathways, and some have been used in surgical applications for decades. Table B represents a comparison of selected skin substitute products on the market today.

TABLE B Selected Skin Substitute Product Comparison

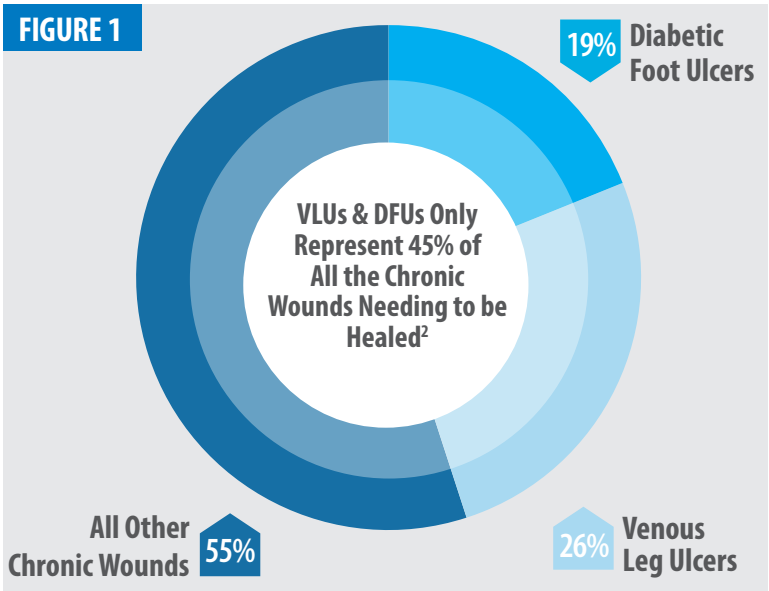
	EpiFix®[6]	Grafix®[8]	Apligraf®[9]	Dermagraft®[10]	TheraSkin®[11]	Graftjacket®[12]
Product description	Dehydrated human amnion/chorion membrane allograft	Cryopreserved amniotic membrane allograft	Bi-layered living skin substitute	Human fibroblast derived dermal substitute	Decellularized dermal matrix	Decellularized dermal matrix
Patient population	Acute & Chronic Wounds	Acute & Chronic Wounds	DFU & VLU ONLY	DFU ONLY	Acute & Chronic Wounds	Acute & Chronic Wounds
Regulatory Pathway	HCT/P 361	HCT/P 361	PMA	PMA	HCT/P 361	HCT/P 361
Product Sizes	Multiple sizes ranging from 14mm diameter disc to 9 X 20 cm^2	Multiple	Only one 44 cm^2 disc	Only one 37.5 cm^2 size	Multiple	Multiple
CMS Approved Applications per Patient	5	TBD	5	8	5	2

In terms of clinical effectiveness, as seen in Table C, some of the newer products have demonstrated an advantage in "time to closure," or the time it takes to heal a wound. For example, in a recent peer reviewed published randomized clinical trial, the MiMedx® EpiFix® amniotic membrane allograft showed an average time to closure of forty-two (42) days[6] in comparison to published data from Shire showing Dermagraft® (which is a PMA product) averaging a time to closure of sixty-five (65) days[9]. Thus, the amniotic membrane allograft product's average time to closure was 44% faster than the PMA product's time to closure. As another example, a recent peer-reviewed poster presented at the leading national wound conference revealed the average cost of EpiFix® per wound (DFUs and VLUs) was $1,562, compared to $8,722 if the wound was treated with human fibroblast derived dermal substitute (Dermagraft®).[5] This equaled approximately an 82% product cost reduction (or $7,160) on average. Thus, not only can many of the newer products result in cost savings because they are more size appropriate and therefore have a low wastage rate, they contribute to additional cost savings because many are more clinically effective than the older products.

TABLE C Independent Clinical Results for Treatment of DFUs

	EpiFix®[6]	Grafix®[8]	Apligraf®[9]	Dermagraft®[10]	TheraSkin®[11]	Graftjacket®[12]
Closure at 4 weeks	77%		20%			37%
Closure at 6 weeks	92%					48%
Closure at 12 weeks	92%	62%	56%	30%	66.7%	69.6%
Time to Closure	42 days	70 days	65 days			
Average Number of Treatments to Closure	2.5	6	4	Not Reported	5	2
Crossover Results	91%[7]	80%				
Healing Endpoint Relative to Control	6 weeks	12 weeks	12 weeks	12 weeks	12 weeks	12 weeks

Finally, while DFUs and VLUs are the two largest single chronic wound types, there are also many other chronic wound types. These other wound types actually represent the majority of all chronic wounds in the United States. A recent study published in the Journal of the American Medical Association (JAMA) showed that from a sample of over 312,000 wounds, 45% of wounds were either DFUs or VLUs, and the other 55% of chronic wounds fell into other categories (See Figure 1).[2] Because Dermagraft® is only indicated for DFUs (19% of the chronic wounds) and Apligraf® is indicated only for DFUs and VLUs, neither are used for the 55% of other chronic wounds that are treated with the other products in the skin substitute category. As Apligraf® and Dermagraft® are not the only two skin substitute products available, it would be a mistake to allow the discussion to center on what is available for the treatment of only two types of chronic wounds when considering the impact of the CMS proposed changes.



Thus, it is clear that there are many clinically effective products available for the treatment of chronic wounds, and Apligraf® and Dermagraft® are not the only products available for treatment. Moreover, Apligraf® and Dermagraft® have never been approved for the treatment of the majority of chronic wounds. Finally, Apligraf® and Dermagraft® are the only products that are offered solely in the single large size, which will become a disadvantage if CMS ceases its practice of reimbursing on a per square centimeter basis. If the CMS proposed rule goes into effect, physicians would still have many clinically effective and cost effective products from which to choose for treatment of the broad array of chronic wounds.

There are Multiple Regulatory Pathways That Chronic Wound Care Products May Take to Market

Shire and Organogenesis also have attempted to distinguish their products from others in the skin substitute category by highlighting the fact that their products came to market ten years ago via a Pre-Market Approval (PMA) process. However, it is important to understand there are multiple regulatory pathways skin substitutes may take to market, and all of them are regulated by the FDA. One route is to qualify for regulation solely under Section 361 of the Public Health Service Act and 21 CFR 1271 in the Code of Federal Regulations, which is the regulatory standard for many human tissue products on the market today. If tissue qualifies for regulation solely under Section 361, it is not required to be "licensed" by the FDA and in fact, no license is available. This is true not just of placental tissue, but also of corneas, dermis, tendon and bone products, most of which also qualify as Section 361 tissue that do not require licenses issued from the FDA. The FDA has determined that a premarket submission proving safety and efficacy are not required for products that qualify for regulation solely under Section 361 as long as they are utilized for homologous uses. Other regulatory pathways, for tissue products that do not meet the standard for regulation solely under Section 361, include approval as a biological product via the FDA's Biologics License Application (BLA) process, a drug under the FDA's New Drug Application (NDA) process, or as a medical device under the FDA's 510(k) or PMA process.

Thus, any argument that the safety and efficacy of a certain product is questionable simply due to the regulatory pathway taken by that product is without merit. The older skin substitutes came to market as medical devices via the PMA process. Due to significant scientific progress in this area in more recent years, newer therapies have come to market via other routes. All of the regulatory avenues are acceptable and legal, so long as a product properly qualifies under the applicable regulations. Thus, while Dermagraft® and Apligraf® may be the only PMA products in the chronic wound care treatment space, that distinction holds no bearing on clinical effectiveness nor should it influence Medicare policy.

In fact, there are products currently available, such as EpiFix®, that are regulated by a non-PMA pathway and are actually more clinically effective than the PMA products.[6]

Conclusion

The skin substitutes market is expanding rapidly, and numerous products that are more cost and clinically effective are now available to treat Medicare beneficiaries.

Ten years ago an argument that Apligraf® and Dermagraft® were the only clinically effective products for chronic wound treatment may have had some merit, as there were relatively few skin substitutes on the market. Today that argument is no longer valid. Additionally, any argument relative to clinical efficacy based on the regulatory pathway a product takes to market is without merit. There are multiple ways a product can be regulated by the FDA, and all of these ways are valid and legal; products taking one regulatory pathway are no safer or efficacious than those taking another based simply on the regulatory pathway taken.

The real issue is wastage, which is clearly demonstrated by CMS data. There are newer skin substitute products that cost less per graft, require fewer applications, and heal wounds more quickly. The older products may be clinically effective and cost effective on larger size wounds, but the majority of wounds are much smaller than the single sizes offered by the older products. Preserving the status quo to protect the older products is an unnecessary and costly step in the wrong direction. MiMedx® supports the CMS proposal to contain costs by packaging the products. Recognizing that wounds do come in various sizes, MiMedx® has encouraged CMS to go one step further and package the products in four tiers according to wound size. MiMedx® estimates this will save CMS in excess of $100M per year in wastage on skin substitutes. This paper focuses on Medicare savings estimates for skin substitute procedures performed in the hospital outpatient setting, but one can further extrapolate the additional savings available to Medicare in the physician office setting, as well as other public programs such as Medicaid and the Veterans Administration. When considering the cumulative effect of reducing waste in these programs and among private health plan as well, the potential magnitude of savings to the entire healthcare system is substantial.

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