ALLIANCE OF
WOUND CARE
STAKEHOLDERS
POWER THROUGH COLLECTIVE ADVOCACY

July 23, 2015

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Submitted electronically to: J11B.Policy@PalmettoGBA.com

RE: DRAFT Local Coverage Determination (LCD) for Application of Skin Substitutes to Lower Extremity Chronic Non Healing Wounds (DL36123)

Dear Dr. Sculimbrene:

On behalf of the Alliance of Wound Care Stakeholders ("Alliance"), we are pleased to submit the following comments in response to the draft local coverage determination for Application of Skin Substitutes to Lower Extremity Chronic Non Healing Wounds ((DL36123)). The Alliance is a nonprofit multidisciplinary trade association of health care professional and patient organizations whose mission is to promote quality care and access to products and services for people with wounds through effective advocacy and educational outreach in the regulatory, legislative, and public arenas. These comments were written with the advice of Alliance clinical specialty societies and organizations that not only possess expert knowledge in complex chronic wounds, but also in wound care research. Many of our members utilize skin substitutes (now known as cellular and/or tissue based products for wounds [CTPs]) in their practices as an adjunctive therapy when treating a patient with a chronic non-healing wound. As such, we have a vested interest in this policy. A list of our members can be found at www.woundcarestakeholders.org.

General Comments

As stated in our specific comments below, the Alliance is concerned with Palmetto using the term "skin substitutes". This term is not a technically accurate term and does not describe the technology that is either currently or will be in the marketplace for products that contain living cells or constitute tissue-based products intended for use in the management, treatment, or healing of skin wounds. Historically, these products have been referred to as "skin substitutes" in reference to their initial use as substitutes for skin grafts in clinical procedures. However, over time, the usage of these products shifted toward chronic ulcers where skin grafts are infrequently used and not standard of care. Moreover, newer products in this category may look nothing like skin and, indeed, have not been designed to function as skin replacements. Thus, there is a need to define terminology in the context of skin wounds as opposed to skin grafting procedures.

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As such, the Alliance recommends that Palmetto adopt the term "Cellular and/or tissue based products for wounds**"** ("CTPs") which does accurately describe and is broad and inclusive of both current and future technology. We would respectfully point out that other organizations, contractors and the wound care clinical community are adopting this verbiage. For instance, American Society of Testing and Materials (ASTM) has created a new draft guidance standard specifically using the CTP nomenclature. In addition, Cigna Government Services is utilizing the term "Cellular and/or Tissue Based Products for Wounds" as the title for its LCD. Historically, the AMA-CPT Editorial Panel intended to change the skin substitute grafting code descriptors in 2012, but AMA was concerned that it would affect Medicare payment and coverage for this work. If the MACs begin referring to these products with correct terminology, we can then request a correction to the CPT® Skin Substitute grafting code descriptors. The Alliance voted to adopt this term in 2013; thus, we will be using the acronym "CTPs" when referring to "Cellular and/or tissue based products for wounds" in this document.

The Alliance recognizes the challenges and difficulties that the A/B MAC contractors such as Palmetto are facing in managing the LCD development process with new CTPs entering the marketplace. We recognize that Palmetto has attempted to establish a fair, balanced and accurate coverage policy. The draft language in the policy gives the appearance that Palmetto will allow expanded treatment options for clinicians based upon providers clinical decision-making by including more CTPs. The Alliance supports this medical decision making approach.

CTP products, as an advanced therapy, have helped our provider members treat patients with chronic wounds that have not progressed to healing [non-healing] despite best standard of care approaches. Therefore clinicians use CTP s for these non-healing wounds to achieve closure and avoid complications.

Based on the title of this LCD, the Alliance questions whether the other types of chronic non healing wounds and acute wounds for which products will covered based on medical necessity since this LCD solely addresses lower extremity wounds, and specifically DFU and VLU. The Alliance believes that since this policy addresses chronic non-healing wounds and while a majority of the chronic wounds may be DFU and VLU, there are other wound types that should be covered based on medical necessity. As such, we recommend that this policy either clearly state that other types of chronic non healing wounds be covered based on medical necessity OR address chronic non healing wounds – defined as those wounds that have not healed within 4 weeks which have not responded to conservative treatment (wounds that may result from trauma, pressure, arterial and/or venous insufficiency, surgery and/or diabetes) and then, change the title of this policy to be more inclusive. Should Palmetto decide to go this route, we would recommend that the title be, "Application of Cellular and/or Tissue Based Products for Wounds (CTPs) for Treatment of Chronic Wounds'

Finally, the Alliance has identified areas in the policy which are confusing and/or contain inconsistent language. We highly recommend that any inconsistencies and/or confusing language be addressed and corrected prior to issuing this policy in final. This is imperative to our member clinicians, since they may be subjected to payment audits based on the provisions contained in this policy.

The Alliance has provided specific comments regarding terminology and inconsistent language below. We have presented them not necessarily in order of importance but in order that they appear in

the draft LCD. The issues are as follows:

Specific Comments

Recommendation for Palmetto to Adopt Term "Cellular and/or Tissue Based Products for Wounds" In Place of 'Skin Substitutes"

While Palmetto has on occasion referred to skin substitutes as "Cellular and Tissue based products" within this LCD, the primary nomenclature used in this policy for these products is still skin substitutes. As mentioned above, the term "skin substitutes" is clinically inaccurate and should be replaced with more inclusive descriptor "Cellular and/or tissue based products for wounds (CTPs)". The term is not a technically accurate and does not describe the technology. Instead, the Alliance recommends that Palmetto adopt the term "Cellular and/or tissue based products for wounds" which does accurately describe all technologies in this sector and is broad and inclusive of both current and future technology. The Alliance adopted this term in 2013; thus, we will be using the acronym "CTPs" when referring to "Cellular and/or tissue based products for wounds" in this document.

The Alliance believes that the term "skin substitute" is misleading and inaccurate to describe the products that are the subject of this LCD for the following reasons:

- This term is not used by either the FDA in its classification of these biologic products nor by CMS in its coding descriptors.

- The CMS HCPCS Work Group abandoned the term "skin substitute" effective in 2010 when a manufacturer requested that CMS delete this term since it was an incorrect descriptor. The manufacturer stated at the 2010 CMS HCPCS Public Meeting that this language was incorrect since allografts are mislabeled as "skin substitutes." Allografts differ in structure, tissue origin, and in some cases differ from biologic products in terms of how they are approved by the FDA (human skin for transplantation not devices). CMS thus changed the descriptors and eliminated the term "skin substitutes" from all of the Q-HCPCS codes for these items.

- In addition, the Agency for Healthcare Research and Quality (AHRQ), in its 2011 draft technology assessment on skin substitutes stated that these products were not "skin substitutes."

In 2012, the Alliance embarked on a yearlong effort to determine an appropriate term. In order to achieve a fair and inclusive process for determining this new term, a workgroup of scientists, clinical organizations, and business entities was created from the Alliance to address this issue. Such diverse multidisciplinary clinical specialties societies as the American Podiatric Medical Association, Society of Vascular Medicine, American College of General Surgeons, Society Association for the Advancement of Wound Care, American Professional Wound Care Association and the American Physical Therapy Association participated in this process.

The following were the criteria used to select the new term:

- be based on science

- be inclusive of all products in marketplace today with eye towards what is in the "pipeline"
- be neutral in regards to FDA--- nothing that would be offensive and not allow manufacturers to get their products approved in the future if needed
- ensure that all products are eligible for Medicare coverage as drugs and biological consistent with their USP monographs
- easily understood by clinicians
- easily linked to the existing CPT codes for the application of the products

The Alliance reviewed over 18 different names during this process and selected the term "Cellular and/or tissue based products for wounds" since it met the criteria listed above. As such, the Alliance recommends that Palmetto not utilize the term "skin substitute" in its policy and instead use the more clinically correct term "cellular and/or tissue based products for wounds (CTPs)."

Coverage Indications, Limitations, and/or Medical Necessity

Skin Grafting or Replacement – Classification of Products

The Alliance believes that the Palmetto policy is problematic in terms of how the products are actually defined. The definitions of "Allografts," "Human Skin Allografts," and "Acellular Matrices" are confusing and misleading. For instance, in the definition of an "Allograft" the draft LCD specifically states "from human skin" which is exactly the same as the fourth category definition of "Human Skin Allograft". The term "Acellular Matrices" is limited to "derived from other than human skin". There are ample acellular matrices derived from human skin (e.g., Graftjacket, DermACELL, and AlloSkin AC]. Furthermore, it is unclear where amniotic products that are acellular [e.g., Epifix (MiMedx), AlloWrap (AlloSource) AmnioCell (DermaSciences), Biovance (Alliqua)] fit in to the classifications/definitions contained in the policy. These products are not composed of skin, but rather amniotic membranes.

The Alliance suggests that if Palmetto is attempting to define the different product types in this product sector within the LCD, that it is done correctly. The Alliance has provided a chart which maybe helpful in assisting you with your definitions and classifications. [Attachment A]

Limitations: Skin Substitutes v Biologic Dressing

The Alliance is concerned and has significant issues with the following language, "all products, unless they are specifically FDA-labeled for use in the types of ulcers considered in this LCD, will be considered to be biologic wound dressings and part of the relevant E/M service provided and not separately payable." The FDA recognizes different regulatory pathways for CTPs: PMA, 510K, HDE, BLA and HCT/Ps. CTPs have different regulatory pathways depending on the source of the tissue. HCT/Ps do not have a specific indication for use like PMA and 510K products. Instead, they have a broad intended use statement. Just because a CTP product is not labeled for use in the types of ulcers listed in this policy – does NOT deem them to be a wound dressing. A CTP promotes wound healing by interacting directly or indirectly with the body tissues. There is direct biological effect in the wound bed as a result. The role of CTPs is not to cover and protect wounds but rather to stimulate endogenous healing, although whether or not an individual CTP is capable of exerting effects on

wound healing must be determined by adequate evidence. Yet, a wound dressing is a material that is utilized for covering and protecting a wound, helping to maintain an optimal wound environment, and shield the wound against the environment without exerting any direct effect in the wound bed. As such, it is not correct for Palmetto to determine that a CTP, which has been cleared as a human HCT/P with the FDA and has broad indications not specified in its labeling, to eliminate its use based on this clearance process, or to designate it as a wound dressing.

The Alliance recommends that Palmetto remove from its LCD the verbiage regarding products not being separately payable and included in the relevant E/M service unless they are labeled for use in the types of ulcers considered in the LCD. Instead, the section should read: "each marketed product is eligible for Medicare reimbursement if it is provided in accordance with its package label or Instructions for Use."

Food and Drug Administration

One area where there is inconsistent language centers on when these products will be considered "reasonable and necessary" and thus covered. For example, Palmetto states that "all products with FDA cleared/approved or designated 361 HCT/P exemption used in accordance with that products' individualized application guidelines will be equally considered for the purpose of this LCD and may be considered reasonable and necessary. However, further in the policy, Palmetto states, "All listed products, unless they are specifically FDA labeled or cleared for use in the types of wounds being treated, will be considered to be biologic dressings and part of the relevant Evaluation and Management (E/M) services provided and not separately reimbursed."

It is our understanding that designated 361 HCT/Ps do not receive FDA labels nor are they cleared for use. So is Palmetto suggesting that 361 HCT/P products will only be considered biologic dressings under this policy? We believe that not only is this inconsistent, but also we are concerned that Palmetto is requiring information that does not exist for some of these products in order for the coverage criteria to be met. As stated below, CTPs have several FDA pathways to enter the market and not all of them require FDA "approval".

For example, PMA and 510K products are approved/cleared with specific indications for use and have FDA approved package labels. These products will receive an approval/clearance letter from the FDA. However, Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) have another FDA pathway, have package instructions for use, but do not receive FDA "approval".

The authority for the HCT/P framework is the Federal Food Drug & Cosmetic Act, which requires premarket clearance or approval for certain products, Sections 351 and 361 of the Public Health Service Act (PHS Act), and 21 CFR 1271, which FDA promulgated to effectuate the requirements for tissue products. The FDA regulatory framework for HCT/Ps has been in place and routinely enforced for years. A product eligible for regulation as a 361 HCT/P solely under Part 1271 is not subject to premarket clearance or approval. To be a 361 HCT/P, the product must meet all four of the following criteria:

1. It is minimally manipulated.
2. It is intended for homologous use as determined by labeling and advertising.

3. Its manufacture does not involve combination with another article, except for water, crystalloids, or a sterilizing, reserving, or storage agent.
4. It does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function.

When developing the regulatory framework for HCT/P products, FDA considered the long history of clinical use of tissue products and the existing body of clinical evidence for human tissue. Based on this body of evidence, the FDA determined that when they are minimally manipulated, intended for a homologous use, not combined with other articles, and do not have a systemic effect, tissue products are ***safe*** and may be marketed and used without any FDA pre-market review, clearance, or approval – thus, they do not have any FDA approved package instructions nor do they receive FDA "approval".

While Palmetto recognizes in the draft policy that HCT/Ps do not require PMA or 510K approval, there is still a statement in the draft policy which seems to preclude these products for reimbursement since they do not receive FDA "approval" for their proposed use.

The Alliance recommends that Palmetto edit the draft policy language to simply delete the information related to biologic dressings. As stated above, none of the products listed are biologic dressings and will help to eliminate the inconsistencies within the policy. The Alliance agrees with the language in which all products with FDA clearance/approval or designated 361 HCT/P exemption used in accordance with that products individualized application guideline will be equally considered.

Podiatrists

The Alliance is concerned that Palmetto will not be providing coverage for the service or the product when they are applied by a podiatrist. The draft LCD states, "Patients receiving a skin substitute graft must be under the care of a physician licensed by the state with full scope of practice for the treatment of their systemic disease process." Furthermore, Palmetto states in the draft policy, "This LCD does not endorse particular products for separate payment so the MD/DO/NPP documentation must support the need for skin replacement surgery and the product used". It may simply be an oversight, however, the Alliance urges Palmetto to recognize podiatrists as providers who can and do treat patients with wounds – especially diabetic foot ulcers.

Requirement That A Patient Is A Non Smoker In Order To Receive Treatment

The Alliance is concerned about language in this draft policy which seems to discriminate against patients who smoke. Specially, we have concerns that if a patient continues to use tobacco products on a regular basis after a 4 week period of conservative wound care, Palmetto is then denying coverage of treatments that could close a patient's wound. This seems to be a bit extreme and without merit. We respectfully request that Palmetto cite the studies/evidence used to make this decision.

We understand and support the efforts to provide counseling, but believe that to deprive patients of these products to help treat their wounds if they are not able to stop smoking will impact patient care. It is interesting to also note that other A/B MAC jurisdictions contained this language in their draft policies but removed this requirement from the final published LCD. The Alliance urges Palmetto to do the same.

Indications for Use – Differentiation between DFU and VLU

Palmetto makes a clear distinction when providing coverage for DFU and VLU. The policy stated that the application of a CTP on a DFU will be covered when the DFU fails to respond to documented conservative measures of greater than 4 weeks. Yet, the policy also states that the application of a CTP on a VLU will be covered when the there has been the presence of a venous stasis ulcer longer than 3 months with failure to respond to conservative treatment after 1 month. It is unclear what evidence Palmetto is using to support their decision to separate the presence of a DFU versus a VLU when the definition of a chronic wound is a wound that has not responded to conservative treatment in 4 weeks. The Alliance does not agree with this distinction and requests that Palmetto provide the evidence supporting this separation. The Alliance knows – based on clinical evidence - that the percentage of change after 4 weeks of healing is a robust indicator of healing at 12 weeks. Delays in alternative or additional therapies contradict prevailing thoughts on ulcer treatment. As such, the Alliance recommends that application of CTPs for both DFU and VLU should be covered when the wound fails to respond to conservative measures after 4 weeks**.**

Limitations/Utilization

The Alliance has significant issues with the utilization section of the LCD. First, Palmetto states that no more than 10 applications for treatment of a single wound within 12 weeks will be permitted. Then, Palmetto states that each of the products identified in the HCPCS code section is eligible for Medicare reimbursement if it is utilized in accordance with its proposed use and in compliance with this LCD. In addition, Palmetto further states that utilization of a CTP that is non compliant with the designated guidelines for that product may necessitate review. Palmetto stresses that products should be utilized in accordance with their guidance. Yet, Palmetto has placed conflicting limitations within the policy.

The FDA labeling for some products requires reapplication every 7 days, while the FDA labeling for other products requires reapplication every 2-3 weeks. So it is very likely if a product requirement is to reapply the product 5 times every 3 weeks – the clinician will be over the number of applications as well as the time frame for the number of weeks permissible under this policy.

Moreover, if the LCD limits treatment to 12 weeks, some of these products will not be able to be used since some of them, according to their FDA labeling, require multiple treatments in a span of time that would exceed 12 weeks. The Alliance is concerned that clinicians would always have to justify utilizing the product chosen to treat their patients – even though they are following the FDA labeling for the products covered under this policy.

The Alliance recommends that Palmetto simply state that the limitations and utilization for a specific product be based upon the labeling of that product. This would be clear for clinicians to understand, not allow for confusion and be in line with the statements Palmetto has made in the document regarding referring to and following FDA guidelines for a specific product.

The Alliance has concerns about the conflicting and confusing language contained in this draft policy in this critical section related to the number of applications. Again, the Alliance recommends that

Palmetto simply revise its policy language to have clinicians follow the FDA labeling with respect to the utilization and application of these products. We also recommend that the documentation in the medical record support the use of the product.

Limitations – Retreatment

The Alliance has an additional issue within this section pertaining to the language that retreatment of a successfully healed ulcer is not covered nor is retreatment of an ulcer following an unsuccessful course of treatment. This is hugely problematic as patients can down the road, due to mechanical issues often not resolvable, develop another ulcer in the same location or can have further breakdown OR can be placed on another type of product after an unsuccessful course of treatment with one type of product. The Alliance does not agree with the language as drafted in this policy as it is not appropriate to eliminate coverage for Medicare beneficiaries if they have further breakdown after a successful treatment of a wound or if a particular product was tried unsuccessfully on a patient and the clinician determines that another product may be used to help heal the wound. We therefore recommend that this language be eliminated from the policy as it is not clinically sound.

Limitations – One product

Furthermore, if a physician begins to utilize one CTP product – with the expectation that the product chosen will work for their patients – yet finds it is unsuccessful, it is unclear under this draft policy whether the clinician can switch to another product. We question whether the draft policy is stating that only one specific CTP can be utilized per episode of care? As a physician, surely the Palmetto Medical Director can recognize that sometimes a treatment option chosen is not successful. This policy seems to be limiting a physician's ability to change course in treating their patients upon the realization that the product chosen is not successfully working in their patient. Also, our members often use one CTP to achieve a certain goal, such as to initiate granulation. Then, depending on the presentation of the wound and the patient's current health status, they may change to another product to close the wound. In order to afford all clinicians the type of autonomy to customize their treatment plan to individual patients that this policy seems to suggest – we recommend allowing treatment according to the FDA label and placing the burden on the physicians to document the need for multiple products.

As such, the Alliance recommends the removal of the following statements, "It is the expectation that only one specific skin substitute graft product will be allowed for the episode of wound are in compliance with FDA guidelines for that specific product not to exceed 10 applications or treatments." A simple statement that the products should be applied in accordance with their FDA labeling places the responsibility on the physician to apply the product correctly and documentation in their files should be sufficient to show that the physician was following guidelines for the product being utilized. If the products are not utilized according to their guidelines – then a physician can and should be placed under prepayment medical review.

Limitations - Combination Therapy

Finally, the Alliance is very concerned with the statement, "combination therapy with any skin substitute (CTP) will be considered not reasonable and necessary. As stated above, Palmetto is placing the onus on the physician to treat patients with the best possible treatment options to optimize outcomes. Yet, in wound care, often Alliance members treat their patients with combinations of therapies to enhance their patients' abilities to heal their wounds. There are instances where the products are used for different purposes. For example, using Integra or Epifix to cover bone in the OR (could even be done in clinic), then another product may be used to close the soft tissue, Dermagraft or Oasis. The Alliance highly suggests eliminating the sentence as it restricts physicians' ability to treat their patients with the best treatment options available.

Clinical Evidence

Palmetto describes when services under this LCD are considered reasonable and necessary but does not describe the specific criteria it will use for determining coverage for any CTP so as to guide the wound care community in its research and publication efforts. This will also allow for a more transparent process for manufacturers when submitting a CTP for coverage.

The Alliance believes that evidence can be established for coverage not only through RCTs but also through registry data, retrospective clinical studies (includes populations of patients with multiple co-morbid conditions that are commonly eliminated in most RCTs), scientific evidence and expert knowledge. This approach is consistent with the widely accepted definition of evidence-based medicine but also adopted by the important organization Patient Centered Outcomes Research Institute (PCORI).

The Alliance does not believe that a policy, which requires much documentation already, should contain language that is subjective at best. We urge you to delete this requirement.

Finally, there needs to be a transparent process in place if coverage would change for a product based on the evidence presented to Palmetto.

Conclusion

On behalf of the Alliance of Wound Care Stakeholders, we appreciate the opportunity to submit these comments. If you have any questions or would like further information, please do not hesitate to contact me.

Sincerely,

Marcia Nusgart R.Ph.

Marcia Nusgart R.Ph.
Executive Director