COALITION OF

Wound Care Manufacturers

March 20, 2013

Dr. James Corcoran
Medical Director
First Coast Service Options, Inc
532 Riverside Avenue
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Jacksonville, FL 32202

RE: Draft LCD - Application of Bioengineered Skin Substitutes for the Treatment of Diabetic and Venous Stasis Ulcers of the Lower Extremities

Dear Dr. Corcoran:

On behalf of the Coalition of Wound Care Manufacturers ("Coalition"), I am pleased to submit the following comments in response to the First Coast Service Option's ("FCSO") draft LCD, "Application of Bioengineered Skin Substitutes for the Treatment of Diabetic and Venous Stasis Ulcers of the Lower Extremities". The Coalition represents leading manufacturers of wound care products used by Medicare beneficiaries for the treatment of wounds including those products that are subject to this draft policy. Since our members have a vested interest in the coverage of these products, this draft policy is of interest and concern to us. The Coalition appreciates the opportunity to offer our comments.

GENERAL COMMENTS

The Coalition recognizes the challenges and difficulties that the A/B MAC contractors such as FCSO are facing in managing the LCD development process with new wound care biologic products entering the marketplace. We know that FCSO has attempted to establish a fair, balanced and accurate coverage policy and has taken into account the various forms of clinical evidence on which to establish coverage for these important wound care biologic products. However, the Coalition has significant issues with this draft policy as our specific comments will reflect.

There are many new products coming into, or already are in, the marketplace which are clinically efficacious as well as cost effective –yet this policy is so limited in the products it does cover that none of these products are covered. It appears that the draft

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policy only covers those products with a 510K or PMA FDA regulatory status and thus ignores additional products that have a regulatory status of HCT/Ps and provide equally clinically effective treatments. The Coalition would like to see more choices available to clinicians to treat their patients.

There are also several inconsistencies in the document that we have identified in our specific comments below. We believe that any inconsistencies need to be addressed and corrected prior to issuing this policy in final.

The Coalition has provided our specific comments below. We have presented them not necessarily in order of importance but in order that they appear in the draft LCD. Our format for addressing them is to state the issue, identify the language in the draft LCD, address our concerns and offer our recommendations. The issues are as follows:

SPECIFIC COMMENTS

Issue 1 - The term "bioengineered skin substitute" is clinically inaccurate and should be replaced with more inclusive descriptor "Cellular and/or tissue based products for wounds (CTPs)".

The Coalition is concerned with FCSO using the term "bioengineered skin substitutes" since it is not a technically accurate term and does not describe the technology that is either currently or will be in the marketplace.

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 regulatory agency--FDA in its classification of these biologic products nor by CMS in its coding descriptors.

- The CMS division that addresses HCPCS coding for these biologic products 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 that this language was wrong 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 its Q 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."

Instead, the Coalition recommends that FCSO adopt the term "Cellular and/or tissue based products for wounds" which does accurately describe and is broad and inclusive of both current and future technology. The Alliance of Wound Care Stakeholders, a multidisciplinary trade association of health care professional and patient organizations whose sole focus is on wound care (including - but not limited to the Society of Vascular Medicine, American Society of General Surgeons, American Podiatric Medical Association, Association for the Advancement of Wound Care, American Professional Wound Care Association) recently voted on adoption of the term Cellular and/or tissue based products for wounds upon careful scientific review. The term met the following criteria:

- based on science
- inclusive of all products in marketplace today with eye towards what is in the "pipeline"
- 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 biologicals consistent with their USP monographs
- easily understood by clinicians
- easily linked to the existing CPT codes for the application of the products

The Coalition agrees with the terminology voted on and adopted by the Alliance. As such, the Coalition recommends that FCSO not utilize the term skin substitute in its policy and use the term cellular and/or tissue based wound care products for wounds (CTPs).

Issue 2 - Omission of Class of CTPs in Draft LCD

Issue: In the "Indications and Limitations of Coverage and/or Medical Necessity" section, FCSO addresses FDA regulation and status of products cleared as PMA and 510k. However, FCSO omitted another class of CTPs termed

"Human Cell Tissues, and Cellular and Tissue-Based Products (HCT/Ps). The FDA Center for Biologics Evaluation and Research (CBER) regulates human tissue for transplantation under the category of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). It is intended for homologous use defined by the FDA for the repair, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor.

We also observe that no HCT/Ps are covered under this draft policy. We believe that the FDA classification system should not be used as a gating factor for coverage decisions. Instead, coverage should be based on the outcome studies and published clinical trials.

Explanation: The FDA regulates HCT/Ps intended for implantation, transplantation, infusion, or transfer into a human recipient. The regulation of these products occurs under a two-tiered, risk-based framework. One major difference between the two tiers is that HCT/Ps regulated under the first tier do not require FDA review or clearance / approval before being marketed. HCT/Ps that fall under the second tier **do** require premarket clearance or approval.

The authority for this 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 14 years.

The overarching policy for this two-tiered framework is that, in 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. However, if the product is more than minimally manipulated there is a higher risk and therefore PMA or 510K approval is required.

Recommendation: The Coalition recommends that HCT/Ps be included in this section and address how these products are regulated under the FDA. As stated above, we believe that the FDA classification system should not be used as a gating factor for coverage decisions. Instead, coverage should be based on the outcome studies.

Issue 3 Limitations – Biologic Wound Dressing Terminology is not correct

Issue*:* FCSO has stated that it would only cover Apligraf, Dermagraft and Oasis products as all other cellular and tissue based wound care products are considered at most "biologic wound dressings". There are many other products that are in the marketplace that are CTPs and they should not be classified as biologic wound dressings as that terminology does not accurately describe the products nor is that terminology used by the FDA or CMS to describe any of the devices or products listed in this draft LCD.

A dressing is a material that is utilized for covering and protecting a wound, although they can be incorporated into the wound, they help shield the wound against the environment without exerting any direct biological effect in the wound bed. Yet products that maintain a "Q Code" all contain viable or non viable cells and/or are derived from biological tissue with intrinsic biological activity, are usually not removed from the wound, are uniquely utilized for their biological influence on the healing process – whether they have a positive influence on the healing process without incorporation OR have the ability to stabilize or support healing through incorporation in whole or part into the regenerating tissue. All the products listed in this draft LCD are CTPs and are NOT wound dressings as they promote wound healing by interacting directly or indirectly with the body tissues.

Language in Draft LCD:

Coverage will not be provided under this LCD for any wound treatment that does not meet the definition of Q4101, Q4102, Q4106 or Q4124. All other such products will be considered to be, at most, "biologic wound dressings." Dressings, by definition, are part of the relevant Evaluation & Management (E/M) service provided and not separately payable.

Concerns: The Coalition disagrees with the terminology that FCSO has used in its draft LCD, to state that coverage will not be provided for products that do not meet the definition of HCPCS codes Q4101, Q4102, Q4106 or Q4124 and that all other products would be considered at most "biologic wound dressings." None of the CTPs included in this draft LCD are biologic wound dressings. They all promote wound healing by interacting directly or indirectly with the body. There is much confusion about the use of these terms which raises the point that FDA and CMS use different terminology to describe these biologic products and cannot be used interchangeably.

It is inaccurate to describe these devices/products as "biologic wound dressings" since this term is neither used by CMS or FDA to describe these biologic products. These are

not “biologic wound dressings” or “surgical dressings” in function or technology. Those dressings are intended to cover a wound, protect from contamination, and to manage the wound condition such as exudate, necrotic tissue or excess dryness. They are not interactive in the wound bed and are identified by CMS in the surgical dressing LCD as “A codes.” On the other hand, the biologic products in this LCD are identified by CMS as “Q codes” - cellular and acellular tissues or cell treatments that interact with the body to enable repair, and are not usually removable.

Furthermore, a product’s eligibility for Medicare coverage purposes depends on (a) whether a product is considered a “drug or biological” under Medicare law, and (b) whether the product otherwise meets the requirements to be covered as a drug or biological provided “incident to” a physician’s service.

Medicare defines the terms “drugs” and “biologicals” as those products that:

… are included (or approved for inclusion) in the United States Pharmacopoeia, the National Formulary1, the United States Homeopathic Pharmacopoeia, or in New Drugs or Accepted Dental Remedies (except for any drugs and biologicals unfavorably evaluated therein), or as are approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital.

Currently, several biologic products are the subject of USP monographs, including but not limited to: Small Intestinal Submucosa Wound Matrix (e.g., OASIS® Wound Matrix and OASIS® Ultra Tri-Layer Matrix), Cryopreserved Human Fibroblast-Derived Dermal Substitute (e.g., Dermagraft), and Graftskin (e.g., Apligraf). As such, these products are eligible for Medicare coverage as a “drug or biological” under Medicare law, notwithstanding FDA’s classification of such products as a “wound dressing”. In addition, other products that have been listed as non covered have USP issued monographs including, but not limited to “Human Acelluar Dermal Matrix” (e.g., Graftjacket® RTM), “Scaffold Human Dermis” (e.g. DermaCell) and “Human Amniotic Membrane Cryopreserved” (e.g. Grafix® PRIME and Grafix® CORE). Therefore, if these products meet the remaining “incident to” requirements, they should be eligible for Medicare coverage.

Recommendation: FCSO should not classify any of the products listed in this draft LCD as “biologic wound dressings” as this description/terminology is simply incorrect. If FCSO is trying to limit the number of products that are covered under this LCD then a better way of doing that is requiring studies to show a products efficacy. Sample language to be added to the LCD could include, “The contractor may determine a product use to be reasonable and necessary for the treatment of wounds or other conditions if, on the basis of available or presented evidence, it is shown to be safe and effective and does

not violate national or local Medicare determinations and regulations. The approval will be limited to specific indications and/or patient populations, practitioner categories, procedures, and/or place of service."

Furthermore, the Coalition recommends, that consistent with Medicare law, if a product has a USP monograph, and meets the requirements to be covered as a biological provided "incident to" a physician's service, the Coalition recommends that those products be covered under your policy. As such, we request that FCSO re-review proposed non-covered items to determine whether they meet the Medicare standard for Part B coverage. We believe that there are other products that in fact do meet the coverage standard and are eligible for coverage under this LCD.

Issue 4 - Indications and limitations for Coverage of covered products

Issue A: Within this section of the draft LCD, FCSO separates out each of the products that are covered and provides their indications for use. However the language contained in this section is not consistent. For example, Apligraf is indicated for partial and/or full thickness venous stasis ulcers, while Oasis is indicated for partial and full thickness wounds. The Coalition believes that this language needs to be consistent and therefore changed.

Language in the Policy:

Apligraf® (Q4101) Indications:
• Full-thickness neuropathic diabetic foot ulcer
• Partial and/or full-thickness venous stasis ulcer

Apligraf® (Q4101) Limitations:
• Apligraf® is limited to five applications per ulcer, although more than three applications to a single wound are usually not expected.
• Retreatment of an ulcer following an unsuccessful course of treatment is not covered.
• Retreatment of a successfully-treated, healed ulcer is not covered.

Oasis® (Q4102; Q4124) Indications:
• Partial and full-thickness neuropathic diabetic foot ulcer.
• Partial and full-thickness venous stasis ulcer.

Oasis® (Q4102; Q4124) Limitations:
• Oasis® is limited to12 weeks of treatment per ulcer.
• Retreatment of an ulcer following an unsuccessful course of treatment is not covered.
• Retreatment of a successfully-treated, healed ulcer is not covered.

Dermagraft® (Q4106) Indications:
• Full thickness diabetic foot ulcers

Dermagraft® (Q4106) Limitations:
• The medical record must document that the twenty-four (24) steps involved in the correct use of this product, as described by clinical trials leading to FDA approval and included in the manufacturer's "Directions for Use" have been followed. The survival of the dermal substitute decreases significantly when the 24 steps in the FDA labeling are not followed.
• Dermagraft® is limited to no more than 8 applications per treatment site over a 12 week period
• Reapplication is not covered for the same ulcer if satisfactory and reasonable healing progress is not noted after 12 weeks of treatment.
• Retreatment of an ulcer following an unsuccessful course of treatment is not covered.
• Retreatment of a successfully-treated, healed ulcer is not covered.

Concerns: The Coalitions concern with this language is that it is not consistent. All of the indications for use of these products should read the same.

Recommendations: The Coalition recommends that the language should read partial and full thickness venous stasis ulcers and partial and full thickness diabetic foot ulcers.

Issue B: The limitations provided in this section of the policy contradict what is written in the utilization guidelines section.

Concerns: The language provided in the limitations section of the policy contradicts what is written in the utilization guidelines section and needs to be clarified prior to the release of this policy in final. Clinicians will not know what to follow.

Recommendation: The Coalition recommends that the limitations in this section be eliminated and that FCSO simply advise clinicians to follow the utilization parameters provided in the FDA labeling and instructions for use for the product being utilized.

Issue 5 – Utilization Guidelines

Issue: This section of the draft policy is completely inconsistent, rather confusing and needs to be rewritten in a clear and concise manner. FCSO states that only a single application of a "skin substitutes" is all that is required to affect wound healing. Then it goes on to say that more than three applications are usually not expected – Four or more applications could result in medical review – five or more is not reasonable and necessary

But Dermagraft is allow no more than 8 applications and Oasis is limited to 12 weeks of treatment. All of this language flies in the face of the instructions for use of the product. Throughout the document, FCSO stresses that these products must be provided and documentation must support FDA labeling requirements for these products. Yet – in this utilization section FCSO strays from the labeling requirements and provides inconsistent, unintelligible utilization requirements.

Language in the Draft: A single application of a bioengineered skin substitute for any particular ulcer is usually all that is required to affect wound healing in those wounds that are likely to be helped by this therapy. More than three applications to a single wound are usually not expected. Four or more applications of a bioengineered skin substitute could result in a medical review for determination of medical necessity. The safety and effectiveness of Apligraf® have not been established for patients receiving more than five device applications. The use of more than five applications for the same ulcer is not considered reasonable and necessary.

The use of Dermagraft® is limited to no more than 8 applications per treatment site over a 12 week period. The use of more than 8 applications for the same ulcer is not considered reasonable and necessary.

Oasis® is limited to12 weeks of treatment per ulcer

Concerns: Any clinician that is trying to figure out the utilization parameters for the products contained in this draft LCD will be utterly confused. All of this language is contrary to the instructions for use of the product. Throughout the document, FCSO stresses that these products must be provided and documentation must support FDA labeling requirements for these products. Yet – in this utilization section FCSO strays from the labeling requirements and provides inconsistent, unintelligible utilization requirements.

Furthermore, the Coalition questions the scientific evidence for the basis that only a single application of a product is all that is required to affect wound healing etc. AHRQ has never addressed utilization in their technology assessments and we are not aware of any evidence that would support this conclusion.

Recommendations: This section is so confusing that the Coalition recommends that the entire section be deleted and rewritten. The Coalition recommends that the utilization guidelines should instead read as follows: "The number of applications is based on the product's instructions for use". This should be reflected in the policy before it becomes final.

On behalf of the Coalition of Wound Care Manufacturers, I appreciate the opportunity to

submit these comments. If you have any questions of would like further information, please do not hesitate to contact me.

Sincerely,

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