ALLIANCE OF
WOUND CARE
STAKEHOLDERS
POWER THROUGH COLLECTIVE ADVOCACY

March 19, 2013

Dr John Corcoran
Medical Director
First Coast Service Options, Inc
532 Riverside Avenue
ROC 19T
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 Alliance of Wound Care Stakeholders ("Alliance"), we are 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 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. A list of our members can be found at www.woundcarestakeholders.org. The Alliance represents every clinical discipline which treats patients with wounds. Our members not only treat patients but conduct clinical research on many of the products that are contained in this draft policy.

GENERAL COMMENTS

As stated in our specific comments below, the Alliance 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. Instead, the Alliance 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 recently voted on adoption of this term and 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 FCSO are facing in managing the LCD development process with new CTPs 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 CTPs. However, this draft policy falls short and the Alliance has significant issues with this draft policy as our specific comments will reflect.

There are many new CTPs coming into the marketplace that are clinically efficacious as well as cost effective –yet this policy is so limited in the products it does cover. In addition, as we state in our specific comments, FCSO has only mentioned and cover products with PMA or 510k regulatory status and ignores those that are HCT/Ps which can also provide clinically effective treatments. We would like to see more choices available to treat 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 Alliance has several issues with this draft policy from terminology used to inconsistent language. 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

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 Alliance 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. Instead, the Alliance 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 recently voted on adoption of this term and we will be using the acronym "CTPs" when referring to Cellular and/or tissue based products for wounds in this document.

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."

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 biologicals 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 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).

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 does 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 Alliance 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.

3. Vague or Inappropriate Language in Indications For Use

Issue: While the Alliance agrees with most of the language contained in the indications for use, we have concerns regarding vague or inappropriate language used for allowing coverage of CTPs. The two concerns are as follows:

1. **Language in the Policy:** For purposes of this LCD, conservative measures include but are not limited to (documentation must indicate that these conditions have been successfully treated and resolved prior to skin substitute treatment)

- Elimination of edema
- Elimination of underlying cellulitis, osteomyelitis or other infection
- Appropriate debridement of necrotic tissue
- For diabetic foot ulcers appropriate non weight bearing and or off loading pressure
- For venous status ulcers standard compression therapy
- Provision of appropriate wound environment to promote wound healing**.**

Concerns: The Alliance's **c**oncern specifically lies with the language "these conditions have been successfully treated and resolved".

Recommendations: The Alliance recommends that the language simply read, "for purposes of this LCD, conservative measures include but are not limited to" and that FCSO eliminate the rest of the sentence prior to the LCD becoming final.

2. **Language in the Policy:** Only apply skin substitutes to wounds with adequate circulation/oxygenation to support tissue growth/wound healing as evidenced by physical examination (presence of acceptable peripheral pulses and or ankle brachial index (ABI) of no less than 0.65).

   Concerns: The Alliance maintains that the language which requests the "presence of acceptable peripheral pulses" is not only vague, but there is no clinical evidence which supports it. As such, the Alliance would like to request that FCSO provide the clinical findings which support the presence of acceptable peripheral pulse.

   Recommendations: The Alliance recommends that FCSO eliminate "presence of acceptable peripheral pulses" from the draft LCD before it becomes final as it is vague and there is no clinical evidence which supports it.

4. Provision of Specific Criteria for Coverage is Necessary

FCSO needs to provide 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 a combination of retrospective clinical studies (relevant since the populations of patients that demonstrate a need for the products in question would be *eliminated* in many and 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 newly created important organization Patient Centered Outcomes Research Institute (PCORI). We believe that payers should cover these CTPs if the manufacturers provide clinical evidence in peer reviewed journals

showing positive outcomes of their products without regard of how they are regulated by the FDA—Class II, III or HCT/Ps. There are examples of A/B MAC policies [NHIC, WPS and Noridian] which have applied this approach and have broader product coverage of CPT products, some with additional indications for wounds with deeper tissue exposure of muscle, tendon and bone, not provided by the First Coast policy.

The Alliance believes that evidence can be established for coverage not only through RCTs but also through a combination of retrospective clinical studies, scientific evidence and expert knowledge. This approach is consistent with the widely accepted definition of evidence based medicine but also adopted by the newly created important organization Patient Centered Outcomes Research Institute (PCORI). We believe that payers should cover these CTPs if the manufacturers provide clinical evidence in peer reviewed journals showing positive outcomes of their products without regard of how they are regulated by the FDA—Class II, III or HCT/Ps.

In addition, as stated in our general comments, we recognize the challenges and difficulties that FCSO is facing in managing the LCD development process with new wound care devices and biologic products entering the marketplace. We recommend that FCSO should consider using the clear format that is used by three other A/B MACs: CGS's **Biologic Products for Wound Treatment and Surgical Interventions**, NHIC's **Biologic Products for Wound Treatment and Surgical Interventions** and NGS's **Biologic Products for Wound Treatment and Surgical Interventions**. Each of these MACs bases its coverage policies on evidence based decision making and clearly addresses the circumstances under which they cover these products and then have policy articles for each product they cover. In addition, the formats are developed with "general indications and limitations to Medicare coverage and payment" and apply them "to all materials and services related to skin substitute/replacement." The more specific coverage information pertaining to the individual biologic products are included in the local coverage articles (LCAs). This type of format should be advantageous to FCSO since the contractor would not need to revise its LCD every time it makes the decision to cover a new biological product; it could merely write a new LCA.

5. Indications and limitations for coverage of products

1. **Issue**: 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 Alliance believes that this language needs to be consistent and therefore changed.

   Language in the Draft LCD:

   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 Alliances concerns are with the inconsistencies of the description of the number of applications. For instance, Apligraf describes applications per ulcer, Oasis describes 12 weeks of applications and Dermagraft describes applications per treatment.

Recommendations: The Alliance recommends that the number of applications should read:
Apligraf- 5 applications
Oasis Wound Matrix and Oasis Ultra Tri-Layer Matrix- 12 applications
Dermagraft- 8 applications

2. **Issue**: An additional issue within this section pertains 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 - 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 on one type of product.

Language in the Policy: Retreatment of an ulcer following an unsuccessful course of treatment is not covered. Retreatment of a successfully treated healed ulcer is not treated.

Recommendations: The Alliance does not agree with the language as drafted in this policy as it is not appropriate to eliminate coverage for a Medicare beneficiary 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.

3. **Issue**: 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 Alliance 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, instructions for use for the product being utilized and the findings of the published clinical trials.

6. Utilization Guidelines

Issue: This section of the draft policy needs to be rewritten in a clear and concise manner. The draft policy is completely inconsistent and rather confusing. 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 allowed 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 and in the findings of the published clinical trials. 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 Alliance 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. FCSO bases coverage on published clinical trials; why would they not use the findings of the published clinical trials to set utilization guidelines?

Recommendations: This section is so confusing that the Alliance recommends that the entire section be deleted and rewritten. The Alliance 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.

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On behalf of the Alliance of Wound Care Manufacturers, we 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,

Marcia Nusgart R.Ph.
Executive Director