American Association of Tissue Banks®

May 31, 2024

CGS Administrators, LLC
Attn: Medical Review
26 Century Blvd., Ste ST610
Nashville, TN 37214-3685

First Coast Service Options, Inc.
Medical Affairs
Suite 100
2020 Technology Parkway
Mechanicsburg, PA 17050

National Government Services, Inc.
Medical Policy Unit
PO Box 7108
Indianapolis, IN 46207-7108

Noridian Healthcare Solutions, LLC
JE and JF Part B Contractor Medical Director(s)
Attention: Draft LCD Comments
PO Box 6781
Fargo, ND 58108-6781

Novitas Solutions, Inc
Medical Affairs
Suite 100
2020 Technology Parkway
Mechanicsburg, PA 17050

Palmetto GBA
Part A Policy
PO Box 100238 (JM) and PO Box 100305 (JJ)
AG-275
Columbia, SC 29202

Wisconsin Physicians Service Insurance Corporation
1717 West Broadway
PO Box 1787
Madison, WI 53701-1787

In Re: LCDs/LCAs – Skin Substitute Grafts/Cellular and Tissue-Based Products (CTPs) for the Treatment of Diabetic Foot Ulcers (DFUs) and Venous Leg Ulcers (VLUs)

To Whom It May Concern:

The American Association of Tissue Banks (AATB or Association) and the American Association of Tissue Banks' Tissue Policy Group (TPG) write to offer comments on the draft local coverage determinations (LCDs) and their associated local coverage articles (LCAs) referenced above. The AATB and TPG urge all seven Medicare Administrative Contractors (MACs) to consider further changes to the application limit; to provide additional clarity on the level of evidence needed for products to be moved from the non-covered list to the covered list; to clarify the process for transitioning from non-covered to covered status; to correct and expand the ICD-10-CM covered list of diagnoses, and to implement a delay in the effective date of the covered product designations to allow manufacturers time to develop the evidence required under the proposed LCDs.

The American Association of Tissue Banks (AATB) is a professional, non-profit, scientific, and educational organization. AATB is the only national tissue banking organization in the United States, and its membership totals more than 120 accredited tissue banks and over 7,000 individual members. These

banks recover tissue from more than 70,000 donors and distribute in excess of 3.3 million allografts for more than 2.5 million tissue transplants performed annually in the US. The overwhelming majority of the human tissue distributed for these transplants comes from AATB-accredited tissue banks.

The AATB TPG includes Chief Executive Officers and senior regulatory personnel from U.S. tissue banks that process donated human tissue. The purpose of the TPG is to drive policy in furtherance of the adoption of laws, regulations, and standards that foster the safety, quality, and availability of donated tissue. The TPG's membership is responsible for the vast majority of tissue available for transplantation within the U.S.

Concerns with application limit: The AATB and TPG appreciate the changes that were made to allow for more than four (4) applications of a skin substitute graft/CTP "in exceptional cases," where documentation of progression of wound closure under the patient's treatment plan and the medical necessity for additional applications has been included. We further appreciate that attestation to the need for additional applications can be done through the reporting of a modifier. We continue to be concerned, however, that the "default" limitation on the number of applications was based on published clinical evidence for a number of products that were used to heal small chronic wounds (i.e. less than 4 sq cm). There is a library of peer-reviewed publications correlating geometry and wound healing (references included below). As such, many chronic wounds will require more than four (4) applications to heal (i.e., larger and more complex wounds), so we encourage you to consider increasing the "default" limit to a number greater than four (4) applications to ensure healing. We agree that the number of applications should be supported by clinical notes in the patient's chart based on the patient's condition, the type of wound (VLU vs DFU), and the medical judgement of the treating physician., We remain concerned with the intent to limit additional applications beyond four (4) to "exceptional cases." While some literature may suggest that the average patient may only need four (4) applications, that implies that about half of patients will need *more* than four (4) applications. We do not believe that a treatment limitation that calibrates roughly half of the patients as incompletely healed should be considered "exceptional," and we are concerned that setting a limit of four (4) applications will discourage clinicians from using additional applications even when medically necessary.

We believe that the LCDs should increase the number of routinely allowable applications, such that applications above the limit would truly be exceptional cases. Without such a change, we are concerned that providers would stop treatment at the four (4) application limit to the detriment of the beneficiaries who need it most: those with large and/or complex wounds and/or patients who are immunocompromised or have severe co-morbidities. We believe that providers should have the CTPs available to them to heal chronic wounds and retain the ability to provide the level of care based on each patient's specific need, including for larger and more complex, chronic wounds.

The AATB and TPG would also appreciate additional clarity on the use of additional applications by reporting of a modifier. Specifically, what are the clinical circumstances under which use of a modifier would be appropriate and how will the modifier be used? In particular, we are concerned that contractors will excessively target claims with modifiers for additional documentation requests and further audit scrutiny – an outcome that would be particularly problematic when the coverage policies do not provide clarity on when additional applications may be covered. We therefore request that contractors clarify how the modifier will be used and what steps contractors will take to limit unnecessary and excessive audit scrutiny.

Clarity on Covered vs. Non-Covered Products: The AATB and TPG additionally note that the LCDs and accompanying LCAs exclude many CTPs from separate coverage and payment, even though these allografts are key medical products that play an important role in the treatment of wounds. Such products, when provided in the form of a sheet, are typically anchored to the wound with sutures, adhesive strips, or other similar mechanisms and provide "scaffolding" at the wound site by providing a temporary extracellular matrix for new cells to attach and grow into during the healing process. Numerous published peer-reviewed prospective multicenter randomized control trials support the use of CTPs in the treatment of DFUs and VLUs versus standard of care (SOC)[1].[2,3,4,5,6,7,8,9,10,11]

The LCDs also note that "coverage will be provided for skin substitute grafts/CTP(s) that have peer-reviewed, published evidence supporting their use as an adjunctive treatment for chronic ulcers shown

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[1] SOC includes treating wounds with actual supplies categorized under A codes rather than skin substitutes categorized under Q codes.

[2]DiDomenico LA, Orgill DP, Galiano RD, et al. Use of an aseptically processed, dehydrated human amnion and chorion membrane improves likelihood and rate of healing in chronic diabetic foot ulcers: A prospective, randomised, multi-centre clinical trial in 80 patients. Int Wound J. 2018;15(6):950-957. doi:10.1111/iwj.12954

[3] Zelen CM, Orgill DP, Serena T, Galiano R, Carter MJ, DiDomenico LA, Keller J, Kaufman J, Li WW. A prospective, randomized, controlled multicenter clinical trial examining healing rates, safety and cost of closure of an acellular reticular allogenic human dermis versus standard of care in the treatment of chronic diabetic foot ulcers. Int Wound J. 2016 Apr 12 doi: 10.1111/iwj.12600

[4] Serena, Thomas E. M.D.; Orgill, Dennis P. M.D., Ph.D.; Armstrong, David G. D.P.M., M.D., Ph.D.; Galiano, Robert D. M.D.; Glat, Paul M. M.D.; Carter, Marissa J. Ph.D.; Kaufman, Jarrod P. M.D.; Li, William W. M.D.; Zelen, Charles M. D.P.M. A Multicenter, Randomized, Controlled, Clinical Trial Evaluating Dehydrated Human Amniotic Membrane in the Treatment of Venous Leg Ulcers. Plastic and Reconstructive Surgery 150(5):p 1128-1136, November 2022. | DOI: 10.1097/PRS.0000000000009650

[5] Zelen CM, Gould L, Serena TE, Carter MJ, Keller J, Li WW. A prospective, randomised, controlled, multi-centre comparative effectiveness study of healing using dehydrated human amnion/chorion membrane allograft, bioengineered skin substitute or standard of care for treatment of chronic lower extremity diabetic ulcers. Int Wound J. 2015;12(6):724-732. doi:10.1111/iwj.12395

[6] Tettelbach W, Cazzell S, Reyzelman AM, Sigal F, Caporusso JM, Agnew PS. A confirmatory study on the efficacy of dehydrated human amnion/chorion membrane dHACM allograft in the management of diabetic foot ulcers: A prospective, multicentre, randomised, controlled study of 110 patients from 14 wound clinics. Int Wound J. 2019;16(1):19-29. doi:10.1111/iwj.12976

[7] Glat, Paul, et al. "Placental membrane provides improved healing efficacy and lower cost versus a tissueengineered human skin in the treatment of diabetic foot ulcerations." Plastic and Reconstructive Surgery Global Open 7.8 (2019).

[8] Guo X, Mu D, Gao F. Efficacy and safety of acellular dermal matrix in diabetic foot ulcer treatment: A systematic review and meta-analysis. Int J Surg. 2017 Apr;40:1-7. doi: 10.1016/j.ijsu.2017.02.008. Epub 2017 Feb 14

[9] Cazzell S, Vayser D, Pham H, Walters J, Reyzelman A, Samsell B, Dorsch K, Moore M. A randomized clinical trial of a human acellular dermal matrix demonstrated superior healing rates for chronic diabetic foot ulcers over conventional care and an active acellular dermal matrix comparator. Wound Repair Regen. 2017 May;25(3):483-497. doi: 10.1111/wrr.12551. Epub 2017 Jun 12.

[10] Reyzelman AM, Bazarov I. Human acellular dermal wound matrix for treatment of DFU: literature review and analysis. J Wound Care. 2015 Mar;24(3):128; 129-34. doi: 10.12968/jowc.2015.24.3.128.

[11] Zelen CM., et al. An Aseptically Processed, Acellular, Reticular, Allogenic Human Dermis Improves Healing in Diabetic Foot Ulcers: A Prospective, Randomised, Controlled, Multi-Centre Follow-Up Trial. Int Wound J. 2018 Apr 22. doi: 10.1111/iwj.12920.

to have failed established methods of healing." Unfortunately, the LCDs do not adequately describe the type of evidence required for products to be added to the covered list. For example, while the LCDs placed significant emphasis on the use of randomized control trials (RCTs) it is not clear if RCTs will be required, or if other types of studies would also qualify. We strongly believe that additional types of data, including real-world data (RWD) and real-world evidence (RWE) should be considered. The American Medical Association House of Delegates (HOD) adopted policy supporting the generation and use of real-world data and real-world evidence fit for regulatory purpose to improve clinical care and patient outcomes.[12] We recommend RWE and RWD should be considered acceptable evidence, and we urge all MACs to clarify in the LCD that such evidence would suffice. Other areas that could benefit from further clarification include requirements around sample size, effect size, power, and acceptable loss to follow-up. Considering how many products currently on the market will not be covered under the proposed policies, the AATB and TPG believe it is critical for the MACs to further describe the level of evidence required for tissue banks and CTP manufacturers to obtain coverage for their products.

Process for Transitioning from Non-Covered to Covered Status: The AATB and TPG highlight that, if these LCDs and accompanying LCAs are finalized, manufacturers will have strong incentives to undertake studies to develop the evidence required under these coverage policies, thereby allowing them to move from non-covered to covered status. We are concerned, however, that detailed product-by-product information included in the LCD will require a full reopening of the LCD through the LCD reconsideration process before products can be moved to covered status. We disagree that such a process should be required, particularly given changes that CMS made to the local coverage determination process in 2018 to remove specific codes and products from LCDs and to move them instead into LCAs.[13] Instead, we believe that, under that process, MACs should be able to make updated determinations about products' coverage status if products fall in line with the stated coverage criteria in the LCD. Furthermore, such determinations should be implemented through updates to LCAs, ideally within 30 days of submission of new evidence.

The AATB and TPG therefore encourage the MACs to clarify the process for products in the non-covered list to move to the covered list, and to specify that the process can be completed in a timely manner through updates to LCAs without requiring reopening of the LCDs. This information is critical as tissue banks contemplate whether to invest in the studies needed to obtain coverage (and whether to invest in future, innovative CTPs). Furthermore, we encourage the MACs to include a clear disclaimer in the LCDs specifying that the evidence summarized in the LCD reflects the current point in time and that as additional evidence arises, such evidence will be used to make determinations about individual products' coverage status irrespective of the evidence documented in the LCD.

Coding concerns: The AATB and TPG also request changes to the covered ICD-10-CM list within the Billing and Coding Article. In particular, we are concerned that EXX.621 includes only diabetic ulcers below the ankle: L97.4X for *heel and midfoot* and L97.5X, of o*ther part of foot* (toes). It is unclear if the MACs intend to limit coverage to exclude diabetic ulcers of the ankle and other parts of the lower limb, or if this is an error in the listing, but we are concerned that the policy will reduce patient access to critical treatments.

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[12] https://www.ama-assn.org/practice-management/digital/physicians-see-big-promise-use-real-world-data-evidence
[13] https://www.cms.gov/newsroom/fact-sheets/summary-significant-changes-medicare-program-integrity-manual-chapter-13-local-coverage

We also note that the non-pressure chronic ulcer codes listed only allow the shallowest ulcers. There are L97.XXX codes that represent ulcers that are deeper, yet do not involve necrosis. These are the patients that may be most critical to receive a CTP as part of limb salvage, and it would be clinically detrimental to exclude these patients.

The AATB and TPG request that the MACs review and expand the ICD-10-CM covered list to address these issues, including by adding the following codes: E08.622; E09.622; E10.622; E11.622; and E13.622; additionally, we urge you to add codes to capture the following levels:

- With muscle involvement without evidence of necrosis;
- With bone involvement without evidence of necrosis; and
- With other specified severity.

Implementation Delay: Given the concerns listed above, and that this is a new requirement, companies need time to gather evidence to support coverage of their products. We request a delay in implementation of the covered / non-covered products' determinations for at least one year after finalization of the LCDs/LCAs. To begin, as noted above, there is not clear guidance on what kind of evidence will be required, in order to design an appropriate study. Additionally, there are a limited number of qualified clinical research organizations (CRO), so it may take time to identify a CRO and complete necessary studies. A delay will allow companies working in good faith to gather required evidence to support coverage of their non-covered products to do so. Moreover, the delay in implementation will provide time for clinicians to shift their patients from non-covered to covered products, as appropriate, and enable companies with products on the covered list to address possible supply chain issues as they seek to make their skin substitutes available to a broader population of patients in need.

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Thank you for taking these comments into consideration. The AATB and TPG stand ready and willing to assist in any way that you deem appropriate.

Respectfully,

Marc Pearce
President & CEO
American Association of Tissue Banks