Novitas Proposed LCD DL35041

Helen Gelly, MD, FUHM, FACHM, UHM/ABPM, FACCWS

Bio

- Wound care as full-time profession since 1991
- Wound care certified
- Published in peer-reviewed journals on Skin Substitutes (CTPs)
- Co-Chair of the UHMS Quality, Utilization, Authorization and Regulatory committee

21st Cures Act

- Summary of evidence considered and a list of the sources
  - STANDARDIZATION OF CLINCIAL EVIDENCE
- Explanation of rationale that supports the determination
- Adherence to the FDA guidelines that are used in the clinical trials that form the basis of the clinical evidence
  - Drugs and Biologicals, Coverage of, for Label and Off-Label Uses
    - **Off-label use is further defined as giving the drug in a way that deviates significantly from the labeled prescribing information for a particular indication.** This includes but is not necessarily limited to, dosage, route of administration, **duration and frequency of administration**, and population to whom the drug would be administered. Drugs used for indications other than those in the approved labeling may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice.
    - https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=33394
- According to DL35041 : Use of skin substitute grafts must meet the medically reasonable and necessary threshold for coverage and these devices must be used in accordance with their approved United States (U.S.) Food and Drug Administration (FDA) intended use.
  - https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39285

Areas of Concern

- Glycemic control parameters
- Limitation of number of applications
- Limitations on size of products
- Smoking status
- Lack of payment policy for the compression wrap that is needed to secure and enhance uptake of these products in VLUs when applied simultaneously
- Place of service and the implications for payment

A1C and Wound Healing

- No differences is wound healing in wounds with a baseline A1C of < 6.5% or >8.0%[1] Fesseha, Betiel K., et al. "Association of hemoglobin A1c and wound healing in diabetic foot ulcers." Diabetes Care 41.7 (2018): 1478-1485.
- Healing occurs at all A1C levels (4.5 – 12.3) but took longer than those with lower A1Cs[2] Markuson, Melanie, et al. "The relationship between hemoglobin A1c values and healing time for lower extremity ulcers in individuals with diabetes." Advances in skin & wound care 22.8 (2009): 365-372.
- No difference in wound sizes in DFU undergoing HBOT in patients with >7% A1c vs < 7% A1C (median 8.05%)[3] Husain, Sharmeen, et al. "Effect of Hemoglobin A1C on Wound Healing in Diabetic Foot Ulcers Treated with Hyperbaric Oxygen Therapy." Journal of the American College of Surgeons 229.4 (2019): S93-S94.
- Picking <7% A1C as cut off is arbitrary, the data shows that high A1Cs reduce the rate of healing, and therefore those patients who have >7% A1C would benefit the most from CTP and advanced modalities to accelerate wound healing and reduce the risk of infection and complications
- Neuropathy is associated more strongly with non-healing and complications in diabetics[4] Domek, Natalie, et al. "Association between hemoglobin A1c and surgical morbidity in elective foot and ankle surgery." The Journal of Foot and Ankle Surgery 55.5 (2016): 939-943.
- 2020 meta-analysis from Johns Hopkins showed that the role of glycemic control in DFU is unclear and that A1C and glucose were not associated with wound healing[5] Lane, Kyrstin L., et al. "Glycemic control and diabetic foot ulcer outcomes: A systematic review and meta-analysis of observational studies." Journal of Diabetes and its Complications 34.10 (2020): 107638

Limitations not related to wound healing

- A1C is paid for only every 90 days by Medicare, so how will Medicare patients, that are getting managed by the PCP, also get frequent enough monitoring to know when they qualify for the suggested 7% cut off? Every A1C is about $66 to the patient that is not covered
- American Geriatrics Society recommends A1C goal of 7.5-8% in older patients with moderate comorbidities
- American Diabetes Association recommends goal of 8-8.5% for older patients with complex medical issues
  - 12.6 Older adults …..with multiple coexisting chronic illnesses, cognitive impairment, or functional dependence should have less stringent glycemic goals (such as A1C <8.0–8.5% [64–69 mmol/mol][4).
- Tight glycemic control in elderly patients with multiple comorbidities increases the chance of life-threatening hypoglycemia and subsequent cardiac and neurological events.

Qaseem, Amir, et al. "Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: a guidance statement update from the American College of Physicians." Annals of internal medicine 168.8 (2018): 569-576.

Cho, Nam Han, et al. "Managing older people with type 2 diabetes." (2013).

Frier, Brian M. "Hypoglycaemia in diabetes mellitus: epidemiology and clinical implications." Nature Reviews Endocrinology 10.12 (2014): 711-722.

[4]American Diabetes Association; 12. Older Adults: Standards of Medical Care in Diabetes—2021. Diabetes Care 1 January 2021; 44 (Supplement_1): S168–S179.

Frequency of Applications

- FDA approval is based on the clinical trials.
- The clinical trials in almost all major CTPS is based on a twelve-week study period and 5-12 applications vs standard of care
  - Apligraf studies: 5 weekly applications
    - Eaglstein, William H., and Vincent Falanga. "Tissue engineering and the development of Apligraf®, a human skin equivalent." Clinical therapeutics 19.5 (1997): 894-905.
  - Graftskin: 5 weekly applications
    - https://doi.org/10.2337/diacare.24.2.290
  - Epifix: 12 weekly applications
    - Bianchi, Christian, et al. "A multicentre randomised controlled trial evaluating the efficacy of dehydrated human amnion/chorion membrane (EpiFix®) allograft for the treatment of venous leg ulcers." International wound journal 15.1 (2018): 114-122.
  - Dermagraft: 8 weekly applications
    - https://doi.org/10.2337/diacare.26.6.1701

Frequency per DL35041: The following are considered not medically reasonable and necessary:

- Greater than two applications of a specific skin substitute graft product within the episode of skin replacement surgery for wound care (defined as 12 weeks from the first application of a skin substitute graft).
  - The expectation is treatment will consist of the fewest repeat applications and amount of product to heal the wound. It is expected that products are used per the labeling. It is not expected that every ulcer, in every patient will require the maximum number of applications listed on the product label. This utilization pattern may be subject to focused medical review.
- Studies cited have NO comment on the number of applications that would be reflected in the above recommendation
  - Pourmousa et al :"EpiFix displayed the highest wound closure rate of 97% at 12 weeks (P=0.00019) in Zelen et al.'s study." Zelen study used 6 applications 2 weeks apart
  - Snyder, D., et al. "Skin substitutes for treating chronic wounds." (2020). No mention was made of any limitations on the number of applications
  - Frykberg RG, Banks J. Management of Diabetic Foot Ulcers: A Review. Fed Pract. 2016;33(2):16-23.

Limitations on Size of products

- Some products only come in one size
- Pricing makes some products unavailable in some sizes depending upon the site of service
- You may need more than 1 piece for one application depending upon the size of the ulcer
- Wastage may be irrelevant in certain clinical scenarios
- You may need 2 pieces of product for one application due to size

HOPD vs Office

- HOPD pays **$4030.36** per application as a facility fee, that included the product, so cost of the product/wastage is immaterial
- The physician gets **$203.57** to apply it in the HOPD
- In the office setting, the physician gets **$347.95** plus the ASP of the product +6% processing fee. (- the sequester again)

In real world patients with VLUs,

~30% of patients have VLUS too numerous to count

How many VLUs are in this picture?

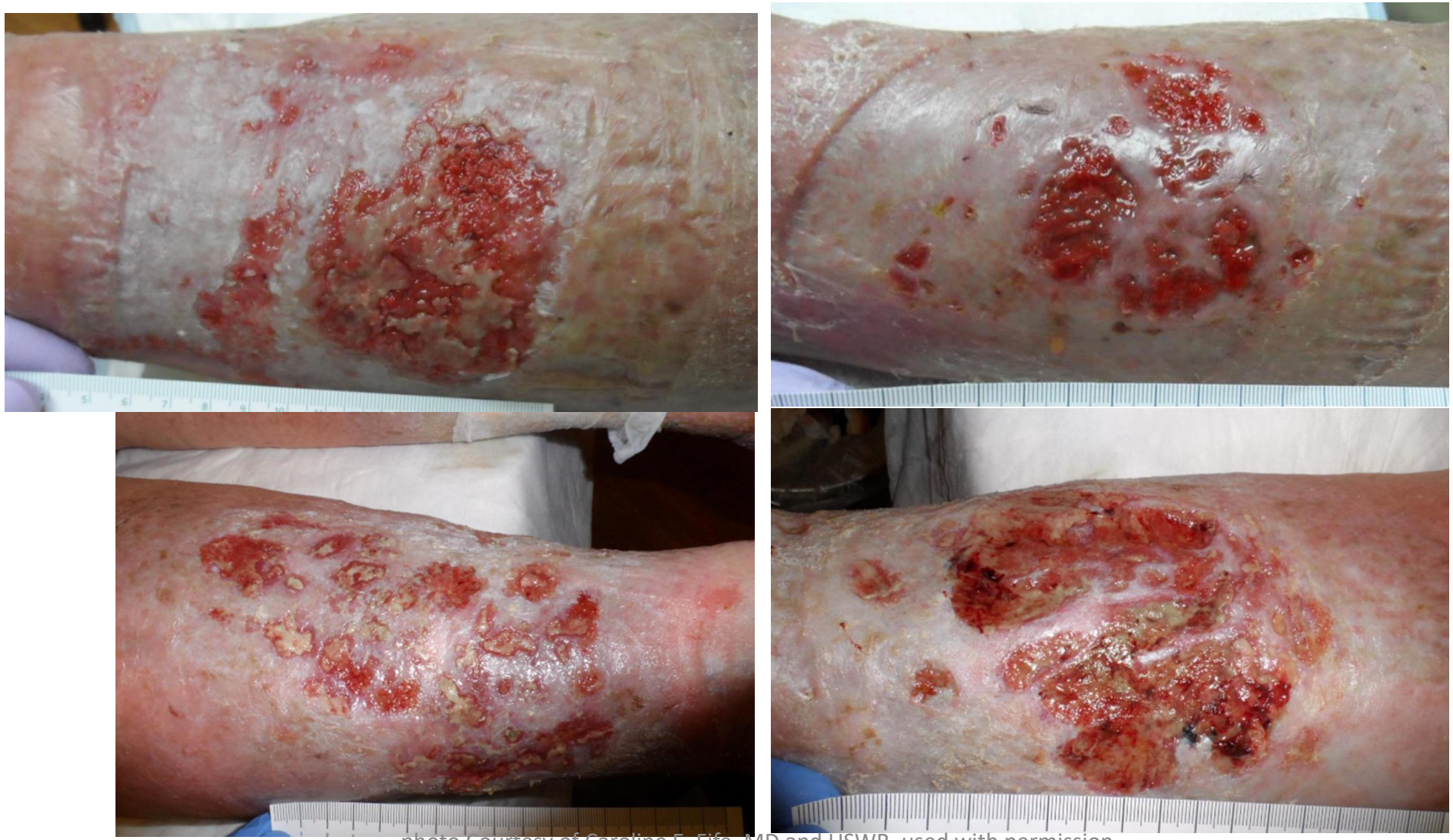

photo Courtesy of Caroline E. Fife, MD and USWR, used with permission

Technically this CTP was placed on two wounds but the smaller one heals (and a new one forms)

photo Courtesy of Caroline E. Fife, MD and USWR, used with permission

What about merged wounds?

The top two merged so now the top one is actually bigger, but he healed the bottom one – is he better?

Photo Courtesy of Caroline E. Fife, MD and USWR, used with permission

What if you can't find the margin? Wounds you can't measure

- Circumferential leg ulcers present continuously for 11 years
- He has an undiagnosed clotting disorder

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Compression wraps

- Every study on venous ulcers has compression wrap (2 or 4 layer) as part of standard of care.
- Compression wraps cost about $16-19 / kit
- NOT included in the office-based practice expense, and not included in the HOPD cost analysis
- Have included gauze and tape as dressing, which is not the standard of care
- In the office setting, this reduces further the reimbursement to the physician as a direct cost that is not accounted for in the CMS practice expense calculation for that procedure

What are the goals of the new draft LCD?

- Contain costs?
  - Proposed parameter are not inline with the FDA approved guidelines
  - If a physician does not practice according to the FDA approved applications schedule, who is medicolegally liable?
- Define an “episode”?
  - Virtually impossible in the venous stasis scenario.
- Unrealistic to expect such tight glycemic control and non-smoking status when similar parameters are not applied to all CMS reimbursed modalities