Wound Care Training Manual

VITALITY
AGELESS CENTER

Purpose

This purpose of this training manual is to provide information and direction for the sale and support of Skin Substitutes for treating chronic wounds. The information presented is to be used as a guide and does not replace need for the provider/customer to conduct their own due diligence, consulting with their respective payors, billing specialists and consultants to verify coding, coverage, payment, or legal advice.

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Properties of Placental Tissue Allografts for Wound Care?

1) The products we feature are primarily DUAL-LAYERED **dehydrated human amnion membrane** (dHAM) allograft composed primarily of a connective tissue matrix. We also offer single layer. The products are minimally manipulated, preserving many of the **natural growth factors** and **cytokines** that are abundantly present in amniotic tissue. The presence of the connective tissue matrix and associated factors help to regenerate soft tissue while inhibiting inflammation and scar tissue formation.
2) The products are amnion containing **no chorion.** (Reactions to chorion include allergic reactions like skin rash, itching or hives, swelling of the face, lips, or tongue, breathing problems, nausea, and vomiting)
3) The products are **dual-sided amnion** that can be placed on either side. (Some competitors must be placed one side down only)
4) **They have strong tensile strength**, making it easier for physicians to handle.
5) Always **ready to use** and have shelf lives of up to 5-years. (Some competitors require cryo freezers and take time to thaw and clean)

Additional Descriptive Bullets

- rich in proteins, growth factors and cytokines which, when applied to a wound to bring down inflammation, breaks up fibrous scar tissue, jumpstarts angiogenesis (blood flow) and signals the body's own progenitor (stem) cells to repair, replace and regenerate soft tissue.
- contains a significant number of cytokines and essential growth factors
- reduces pain when applied to a wound
- increases and enhances the wound healing process
- has antibacterial properties
- is non-immunogenic (will not be seen as foreign material)
- provides a biological barrier
- provides a matrix for migration and proliferation of cells
- reduces inflammation
- reduces scar tissue formation
- terminally sterilized to create an acellular product and ensure patient safety

Main Priorities for Practitioners

1. Is it reimbursable? Yes – our focus is Medicare and Medicare Replacement.
2. Is it FDA approved? It is FDA 361 cleared which precludes the need for an approval for marketing and use. These allografts have been widely used for decades and are well reimbursed.
3. Are there Medicare Guidelines or Local Coverage Determinations (LCDs)? Yes. This is a very significant fact. Providers prefer to have documented guidelines from Medicare with specific direction for indicated uses/coding/documentation. It provides a high level of assurance that if they follow the Medicare guidelines, they will be safe with their reimbursement.
4. Is your products listed on the National Medicare ASP Reimbursement Fee Schedule?

They have to be able to use the product and that's why these are the priorities.

Wound Care Basics

- Definitions
  - Necrosis – dead tissue, doesn't come back to life (black tissue)
  - Bioburden – gelatinized fluid that needs to come out to allow healing
  - Inflammation – Redness and pain (can have inflammation without infection)
  - Edema – swelling or water retention
  - Pressure offloading – devices utilized
  - Granulation – red velvety tissue that skin grows on. Fertilizer that grows the grass. Need granulation for healing
  - Epithelization – skin growing on the granulation tissue (yellow tissue)
  - Chronic wound – not progressing through normal healing process – generally speaking if the wound is not healing after a month it is considered a **chronic wound**
  - Debridement – removal of non-viable tissue
- Normal Wound Healing Stages
    1. **Hemostasis** – close by clotting
    2. **Inflammation** – natural part of wound healing – but need to progress past this phase. Is typically the phase that a wound can get stalled in rendering it chronic.
    3. **Proliferative** – all of the fibroblasts come in to start making a structure – wound starts to contract and fills in
    4. **Remodeling** – granulation and stops growing – allow granulation tissue to grow on the scaffolding
  - If the wound is rendered "chronic" the question is: "Where are we in the wound healing phase and where is it stuck?"
- Acute vs Chronic Wounds
  - Will you start with the wound and slap a product on it? No - you see where it is in the process. If the wound is progressing, you let that happen. If stuck somewhere in a healing phases then advanced wound care products, can be used. More specifics on this below.
  - We concentrate on wounds that are not progressing – Chronic >30 days.
- Global Wound Complications
    1. Infections
    2. Fluid loss
    3. Temperature loss
    4. Debility
  - Infections – leave a wound open long enough its going to infect – increased pain, swelling, redness and drainage – yellow/green discharge – complications = sepsis, limb loss
  - Fluid loss – dehydration reduces the body's blood volume, reduce oxygen and nutrient delivery to the wound bed – impairs wound healing – interrupts cell function. Patients with burns lose large amounts of water through

evaporation from open wounds. Wound covering is the first line of defense for maintenance of body fluid balance (important to know for burn wound care).
    - Temperature loss – Not as big an issue for local/smaller wounds
    - Debility – Inability to work (can't bare weight on their foot/wound) – Pain (quality of life issue – biggest complaint – significant issue – can't function) – Immobilization (diff wounds require immobilization for off loading – compliance issue) – Mental and Emotional (psychological impact is severe – depression – loneliness – impact on social life – empathy) – Inhibits quality of life
- Wound types
    - Pressure ulcer – usually for bed ridden patients or in wheelchairs – biggest thing that needs to be done is pressure off-loading. Grafts may stimulate tissue growth, but most important treatment is pressure off-loading.
    - Venous ulcer – Occur due to venous hypertension from malfunctioning veins. The high pressure causes the wounds to keep from healing. Veins have valves in them – if the valves are not working the blood will fall backwards with gravity. First and primary treatment = compression. Will not heal until you get rid of that venous hypertension.
    - Diabetic foot ulcer – Very difficult wound to heal due to multiple different issues. Pressure causes these. Usually starts with trauma – i.e. step on something. Diabetes complicates the healing/neuropathy/etc – don't have feeling in the foot. They use antibiotics and does nothing. White stuff is macerated tissue. Need to absorb the drainage. Are you staying off your feet (pressure off-loading)? Pressure off-loading helps.
    - Surgical wounds – Mostly from an incision separating (Dehiscence) or from infection or poor healing. Acute wound may not heal in 4 weeks. Treat different wounds differently.
    - Trauma leg wounds – these can be extremely variable but constitute a large # of wounds. Need to clear out all of the bad stuff and get to the bottom to see what you have.
    - Burn wound – damage from heat/sun/rad.
    - Hematoma – necrosis on top – remove it – find hematoma (usually large below the necrotic tissue); work your way down and see what you have. Can't just treat the top of it – remove and work your way down.
    - Gangrene – necrosis in your foot or finger.
- Complications of open wounds
    - Osteomyelitis – bone exposed creating infection – have to do something with the bone – pressure off loading or removal.
    - Peri wound dermatitis – irritated tissue – allergic reaction causing dermatitis and eating the skin around the wound. Have to figure out what is causing it and fix it.

- Infection & Biofilm
- Systemic treatment - part of overall wound care
  - Nutrition – protein necessary for wound healing. Must be assessed and addressed or wound healing will be delayed.
  - Trauma and Surgical Care – Surgical intervention is used when significant tissue loss or infection is noted. Must debride thoroughly first.
  - Disease Control
    - Arterial disease
      - Need blood flow to heal wounds
      - Assess it
      - If you debride a wound without good blood flow you just make it bigger
      - Check blood pressure at their ankle (numerator) and arm (denominator)
    - Venous pressure relief
      - Work up
      - Edema control
      - Ablation – cauterize the vein to address venous hypertension (see above notes on Venous Ulcers). Use catheter in procedure.
    - Blood Glucose control (for Diabetic Foot Ulcers)
      - High blood sugar decrease healing
      - Monitor Hg A1C (Hemoglobin A1C) for DM control. Normal <6.2. If 9 or 16… May not come down right away even if you manage sugar.
      - **WILL THE PRODUCT WORK IF YOU DON'T HAVE THE HIGH BLOOD SUGAR UNDER CONTROL? Understand that this must be addressed. Will the doc choose to use the product? Will it help? Maybe but just understand that this standard of care has to be addressed.**
    - Other medical pathologies
      - Autoimmune disease – Vasculitis most commonly seen in Dr. Medley's practice. This causes a chronic wound.
      - Skin cancer
  - **Normal Standard of Care** - Need to follow the normal standard of care and clear the way before you use a product. See the wound after debridement. Address venous….compression….off-loading etc.
    - **FOLLOW <u>NORMAL STANDARD OF CARE</u> (NSOC) BEFORE YOU USE THE PRODUCT. WHEN TALK TO THE CLINICIAN – HAVE YOU DONE EVERYTHING POSSIBLE AND FOLLOWED NORMAL STANDARD OF CARE PRIOR TO USING THE PRODUCT?**

        - **EXHAUST NSOC TREATMENTS BEFORE YOU USE THE PRODUCT.**
        - **IF THE WOUND IS CHRONIC, WHERE IS THE WOUND STUCK AND WILL THE PRODUCT HELP AND/OR WHAT ELSE NEEDS TO HAPPEN. i.e. inflammation is part of the healing process but if the wound is stuck at the inflammatory phase what needs to be done to make it progress?**
- Infection Control
    - Important part of the NSOC. Some docs will use anti-biotics but if the actual organism is not identified through culture or PCR testing then the anti-biotics may not work.
    - There are multiple products on the market to control infection and Biofilm.
    - What if a wound is healing even though there are bacteria present? Do you use antibiotics to address the bacteria? No, you don't need to. We have lots of bacteria in our bodies. If the bacteria are not stalling the healing process, then you don't need to. Treat infections for sure prior to use of our product because it won't heal if you don't.
- Local Wound Care
    - Surgical
        - Debridement – sharp – blunt - ultrasound
        - Incision and Drainage - abscess
        - Excision – i.e. skin cancer/MOHS
        - Biopsy – used to help diagnose diff wounds with unique characteristics
        - Skin grafting
        - Primary and secondary closure – closing wound is seldom successful but many try – secondary is to allow it to health with local wound care.
        - Various local treatments
            - Chemical debridement – Enzymatic
            - Prizma/Promogran
            - Intestinal matrix
            - Other ….
- Wound dressings
    - Moisten – don't want it too moist or too dry
    - Absorbent
    - Antimicrobial
    - Iodine/Silver based
    - Non-stick

        - Goal – Provide best wound environment for healing depending on what is currently happening with the wound. This changes frequently with the same wound.
    - Growth Factors and Biologic Products – Growth Factors – Cytokines
    - Skin Substitutes – Growth Factors/Placental Tissue/Cellular Products/Collagen Matrix/UBM's (Urinary Bladder Matrix-Bovine/Porcine)

When are Placental Derived Amnion Allografts & other CTP's Appropriate to Use for Treatment & Reimbursement?

- In order to be reimbursed, follow **Medicare Guidelines / LCD's** for types of wounds indicated for use and guidelines for when you can use CTPs (Cellular and/or Tissue Based Products).
- Local Coverage Determinations (LCDs) are published by Medicare Contractors. Medicare Contractors are private entities (usually major insurance companies) that receive a contract from Medicare to service (benefits, claims, etc) providers and beneficiaries in a given state/s. Published LCDs give providers/practices/doctors much confidence because they provide specific Medicare guidance as to how and when the provider can bill for a product or service. There are published LCD's that cover wound care products specific to VLU/DFUs. As noted above this is very important and appreciated by the provider. The LCDs are available in Dropbox - read them.
- Types of wounds in the guidelines - and thus our focus:
  - Diabetic Foot Ulcers (DFUs)
  - Venous Stasis Leg Ulcers (VLUs)
  - Some LCDs also refer to Pressure Ulcers and Arterial Ulcers.
- When can the doctor use CTPs to treat DFU/VLUs?

  After following the **Normal Standard of Care (NSOC)** "Chronic wounds have failed to pass through the normal healing process in an orderly and timely manner and often remain in the inflammation phase. A wound may be considered **chronic** if it has not entered the proliferation phase after **4 weeks** of therapy [for **DFUs**] [and **4-6 weeks** of NSOC for **VLUs**]"

  "Four weeks of standard of care without achieving a 50 percent reduction in wound size may signal the need for a change or additional therapies."

  "If **chronic** wounds fail to respond to standard of care, skin substitutes may be used as an adjunct to establish chronic wound care methods to increase the likelihood of complete healing."

  CMS website article: Skin Substitutes for Treating Chronic Wounds – Technical Brief, Project IND: WNDT0818, February 2, 2020 (Prepared for HHS)

  Summary: Following Medicare Guidelines, the CTP may be used and reimbursed after NSOC has been exhausted and applied.

- Is the **Normal Standard of Care** the same for DLU's and VLU's? No, VLU's focus on venous insufficiency (blood circulation) and while many components of

NSOC are shared with DLU's the difference is a focus on circulatory therapy including compression therapy, ablations if necessary, and other venous therapy. DLU's differ in that the focus is on pressure off-loading, blood glucose control and other diabetic complications. NSOC for both wounds would include wound debridement, biofilm & infection control, nutrition/protein and other local wound care management.

Normal Standard of Care

Including:

1. Wound debridement
2. Treatment of Systemic issues including Glucose control
3. Pressure off-loading for DFU
4. Evaluation and treatment of vascular disease, venous and arterial
5. Treating infection
6. Local wound care management
7. Nutritional

Advanced wound care products may be appropriate after conservative treatment has been exhausted and the patient's wound is not responding.

Standard of Care

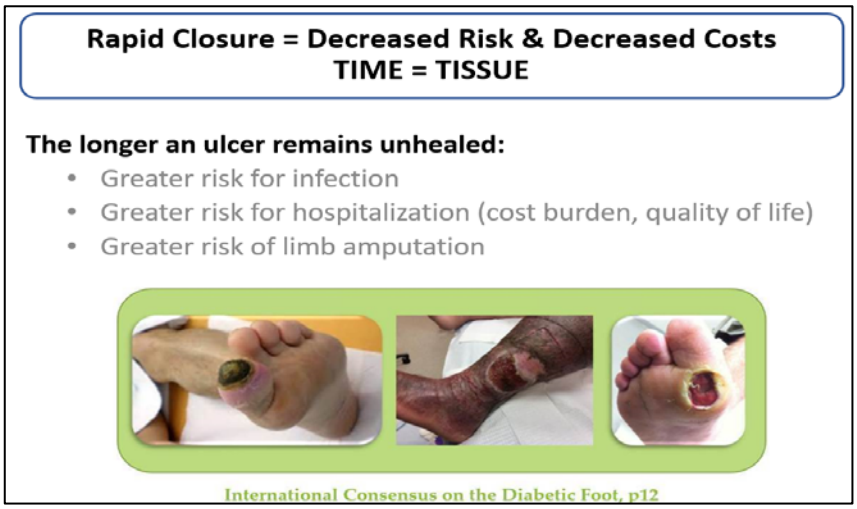
Medical records document that conservative pre-treatment wound management has been tried and failed to induce healing.
Standard of care at least 30 days DFU, 30-45 days VLU.

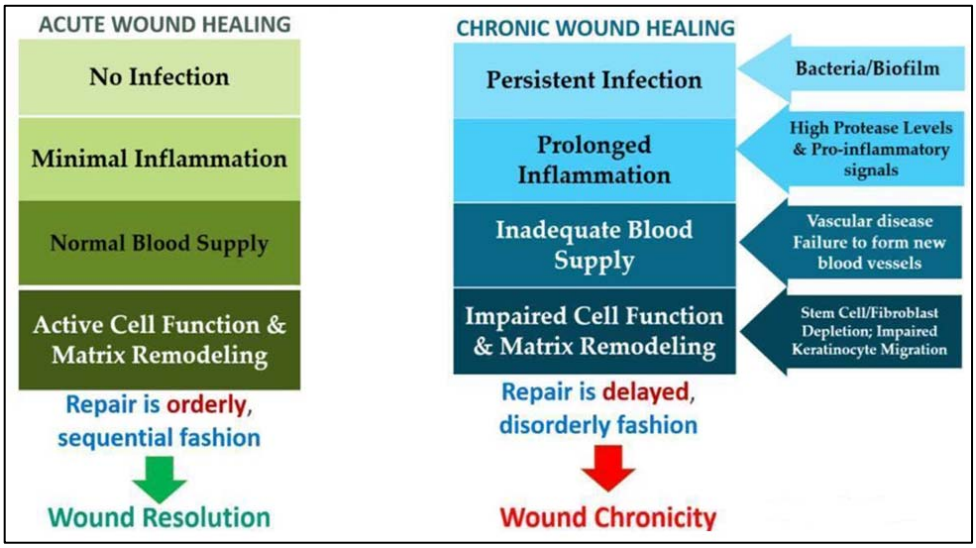
Protocol for the use of advanced wound care product published by CMO of one manufacturer:

Standard of Care – General All Wounds	+ Standard of Care – Venus Stasis Wound	+ Standard of Care – Diabetic Wound
• Drainage controlled • Local wound care environment addressed • Cultures taken and Infection treated • Debridement; sharp or enzymatic as often as needed • Nutritional assessment and supplementation as needed • Systemic pathology addressed and currently under treatment	• Venous incompetence study to evaluate for reflux • Arterial study to assess perfusion • Venous ablation as needed for venous hypertension • Edema control with compression and elevation • Address systemic factors affecting edema • Drainage controlled 	• Arterial study to assess perfusion • Assess diabetic control and refer appropriately • Appropriate pressure offloading 

The Stalled Wound	Indication for use of advanced wound care product
• Standard wound care has been used. • There is a lack of wound improvement despite the standard of care discussed above. (i.e.infection, necrosis, excess drainage, and pressure) • Wound base lacks growth clinically. • Wound is likely halted in the inflammatory stage.	• To use when wound is stalled – as previously defined. • Apply to stimulate growth through providing a better wound environment and helping the wound heal itself. • All other current therapy must continue for best success. • Most insurances typically require documentation of standard of care treatment. If you can document that this standard of care treatment was done prior to your evaluation, then you may proceed with the application of the advanced wound care product.

- Why not do NSOC for 60-90-120+ days? Because if a wound is stalled and not healing, continuous debridement of non-viable tissue, as an example, simply increases the wound size. The wound is not improving and will worsen. The longer a wound is open, the more serious it becomes and the harder it is to close it. So no, more standard of care is not better if the wound is stalled and not healing. The industry and Medicare recognize this and also understand that chronic non-healing wounds often lead to hospitalizations and amputations. Major amputations come with a mortality rate of 2 years on average. The cost of a chronic non-healing wound can accelerate to very large numbers the longer it is open. This is why Medicare will pay for advanced wound care products like once the NSOC is completed and has not induced healing.TIMING IS IMPORTANT. If the NSOC yields results and the wound is closing within the industry standard of 50%, give or take, then there is no need for our product. Your customer will have a mix of wounds that respond to NSOC and wounds that do not. Our graft is appropriate and reimbursable for the latter patient wounds.





Eming et al. Sci Transl Med 2014

General Treatment Protocol

- See the Membrane Wrap, X Wrap, Restorigen Graft™ IFU (Instructions for Use PDF).
- There is of course variations to application but this provides you with one popular approach.
- Once the practitioner determines the need for a CTP and chooses our product, they will:
    - order the appropriate size graft for the wound.
    - prepare the wound
    - apply the graft to the wound
    - cover the graft with a silicone perforated bandage (i.e. Mepitel or Adaptic) and affix with steri-strips.
    - Apply non-stick sectional bandages on top to pressurize and keep the application in place.
    - wrap with a compression bandage and send the patient home with instructions to keep the wound dry and instructions to continue the NSOC protocols (the NSOC does not end just because they are using our product).
    - Typically, the doctor will have the patient back every 7 days for a new graft application until the wound closes.
    - The graft provides coverage to protect the wound from heat and moisture loss (an essential requirement of any wound care covering). In addition, The growth factors, proteins and cytokines inherent in the graft help to provide stimulation of new tissue growth. The GF/P/C can help to supercharge the wound and move it forward from the inflammatory phase that the chronic wound stalled in.
    - Typically, in 80-85%+ of **chronic** DLU's and VLU's, the graft will help close the wound in 4-8 applications.
    - Is there a limit to how many grafts can be used and reimbursed? The general Medicare Contractor guideline is reimbursement for up to 10 grafts or 12 weeks of applications per wound per year as long as the product is improving the wound. We work with providers that have done more due to progress after the 10th and so on.