Skin Substitutes for Chronic Wounds

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Policy contains: diabetic foot ulcer, skin substitutes (cellular, acellular), venous leg ulcer, thermal burns.

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Coverage policy

Skin substitutes (i.e.,cellular or acellular products) are clinically proven and, therefore, may be medically necessary for cutaneous wounds and thermal burns when all general and indication-specific criteria below are met:

General (all indications)

- Coverage is contingent upon meeting all of the following general criteria:
- Partial or full-thickness cutaneous defect with a prepared wound bed (adequate debridement, clean, moisture-balanced) and no clinical signs of active infection (Eriksson, 2022).
- Managing the specific cause of the wound is required during treatment. This includes proven offloading (using a special cast, boot, or other device to take all pressure off the wound) for diabetic foot ulcers, and sustained compression (using special tight bandages or socks) for venous leg ulcers (Bus, 2024; Wound, Ostomy, and Continence Nurses Society, 2021).
- Nutritional status has been assessed and optimized to support healing (Eriksson, 2022).
- Objective perfusion assessment supports healing potential as defined for the specific indication below.
- One product at a time; no known hypersensitivity to the product source (Eriksson, 2022).
- The application technique and frequency must conform to the Food and Drug Administration-labeled instructions for use for the selected product.

Diabetic foot ulcers (neuropathic, non-ischemic)
Adjunctive use of cellular or acellular skin substitute products to promote ulcer closure is clinically proven and, therefore, may be medically necessary when all general criteria are met and:

- Adequate perfusion is documented: Suggested by any of toe pressure ≥ 30 mm Hg, skin perfusion pressure ≥ 40 mm Hg, or transcutaneous oxygen pressure > 25 mm Hg. Urgent vascular imaging and consultation for revascularization must be considered if ankle pressure is <50 mm Hg, ankle-brachial index is < 0.5, toe pressure is < 30 mm Hg, or transcutaneous oxygen pressure is < 25 mm Hg. Ankle-brachial index alone is unreliable in diabetes (Fitridge, 2023; Hinchliffe, 2020).
- The ulcer is a chronic, non-infected ulcer that extends through the dermis without exposed tendon, muscle, capsule, or bone. It has failed to show ≥ 50% area reduction after ≥4 weeks of optimized standard care (serial debridement, moisture balance, infection control, and effective offloading). The wound must also meet the minimum chronicity duration specified in the selected product's labeling (e.g., greater than 3 weeks for Apligraf; greater than 6 weeks for Dermagraft) (Lavery, 2024; International Working Group on the Diabetic Foot, 2023).
- Glycemic management is being addressed and optimized (Lavery, 2024).
- No untreated osteomyelitis at the ulcer site and no active Charcot process involving the ulcer surface. Manage infection or Charcot before applying a skin substitute (Lavery, 2024; International Working Group on the Diabetic Foot, 2023).

Nonhealing dermal wounds (non-pressure)

Adjunctive use of cellular or acellular skin substitute products is clinically proven and, therefore, may be medically necessary when all general criteria are met and:

- Adequate perfusion is documented: Suggested by any of toe pressure ≥ 30 mm Hg, skin perfusion pressure ≥ 40 mm Hg, or transcutaneous oxygen pressure ≥ 25 mm Hg. Urgent vascular imaging and consultation for revascularization must be considered if ankle pressure is < 50 mm Hg, ankle-brachial index is < 0.5, toe pressure is < 30 mm Hg, or transcutaneous oxygen pressure is < 25 mm Hg. Ankle-brachial index alone may be unreliable in diabetes (Fitridge, 2023; Hinchliffe, 2020).
- Non-infected, partial- or full-thickness traumatic, postsurgical, or ischemic venous mixed ulcers fail to improve after more than 4 weeks of optimized care as above. Selection should follow labeling and objective monitoring (Eriksson, 2022).

Thermal burns

Use of skin substitute products in acute thermal burns is clinically proven and, therefore, may be medically necessary when all general criteria are met and:

- Partial- or deep partial-thickness thermal burns have undergone appropriate excision and hemostasis; no burn wound infection is present; autograft is not immediately available or is being staged; products are used for temporary coverage, donor-site optimization, or to reduce autograft burden per labeling and evidence (Hicks 2019; van den Bosch, 2025).

Venous leg ulcers

Adjunctive use of cellular or acellular skin substitute products with sustained therapeutic compression is clinically proven and, therefore, may be medically necessary when all general criteria are met and:

- Adequate arterial perfusion is confirmed: Apply standard compression if ankle-brachial index is ≥ 0.8; consider modified/light compression if ankle-brachial index is 0.5–0.8; do not initiate compression if ankle-brachial index is < 0.5 or > 1.3 (Wound, Ostomy, and Continence Nurses Society, 2021).
- A chronic, non-infected partial or full-thickness ulcer has failed to show meaningful improvement (e.g., <50% area reduction) after ≥ 4 weeks of optimized standard care with sustained therapeutic compression, appropriate debridement, infection control, and moisture balance (O'Donnell, 2014; Marston, 2016; Wound, Ostomy, and Continence Nurses Society, 2021).
- Sustained therapeutic compression must continue during treatment (O'Donnell, 2014; Wound, Ostomy, and Continence Nurses Society, 2021).

See the Appendix for representative products by class and the indications covered under this policy; examples are provided for illustrative purposes.

Limitations

Other uses of skin substitute products are investigational/not clinically proven and, therefore, not medically necessary, including for the following:

- In those without documented offloading for a diabetic foot ulcer (Lavery, 2024) or without sustained therapeutic compression for a venous leg ulcer (O'Donnell, 2014).
- Those with uncontrolled infection, untreated ischemia below the thresholds defined in the indication-specific criteria, or an unprepared wound bed (Hinchliffe, 2020), and those with known hypersensitivity to the product source (Snyder, 2020).
- For active vasculitides or autoimmune ulcerative conditions requiring primary systemic management (Eriksson, 2022).
- For routine use for pressure ulcers (Gould, 2024).
- For prophylactic use on closed, intact skin or for cosmetic purposes (Snyder, 2020).
- Use on fully epithelialized wounds is also not medically necessary (Snyder, 2020).
- When more than one product is used simultaneously on the same wound (Snyder, 2020).
- If there is less than 50% area reduction after 4 weeks of product use, this indicates a need to change the approach (Lavery, 2024).

Alternative covered services

- Optimized standard wound care: regular debridement, moisture balance, appropriate dressings.
- Offloading for diabetic foot ulcer: total contact casting or other irremovable knee-high devices when feasible.
- Compression therapy for venous leg ulcer: sustained, multilayer compression with edema control.
- Infection management: culture-guided therapy and source control; treat osteomyelitis when present.
- Vascular assessment and optimization, including revascularization when indicated by perfusion thresholds above.
- Metabolic and risk modification: glycemic management, smoking cessation, and nutrition optimization.
- Adjuncts for wound bed preparation: negative pressure wound therapy and biofilm control as indicated.

Background

Chronic wounds, including diabetic foot ulcers, venous or arterial ulcers, neuropathic ulcers, and pressure ulcers, persist beyond four to six weeks and often fail to reduce in size with standard wound care. These wounds are common (affecting roughly 2 % of the U.S. population). Because chronic wounds do not heal properly,

complications such as infection, osteomyelitis, amputation, and sepsis arise; mortality rates for diabetic foot ulcers can be comparable to those of some cancers. Skin substitutes are considered advanced therapies rather than first-line treatments (Vecin, 2023).

Skin and soft tissue substitutes are a diverse group of materials designed to promote wound healing and restore the structural and functional integrity of the skin and soft tissue. They are utilized when standard wound care fails or autologous grafting is infeasible. These products function by providing a protective barrier, maintaining moisture, and offering a scaffold, growth factors, or cellular components that support tissue regeneration. Chronic wounds, such as diabetic foot ulcers and venous leg ulcers, along with acute wounds like thermal burns, present significant clinical challenges and disease burden (Halim, 2010)

A skin substitute is defined as a cellular (containing living cells) or acellular (without living cells) matrix. Sources include human tissue (autologous or allogeneic, such as cadaveric dermis or amniotic/chorionic membranes), non-human tissue (xenographic, such as porcine or bovine sources), synthetic polymers, or biosynthetic composites (Capo 2014; Vecin, 2023). Products are further categorized by the layers they replace (dermal, epidermal, or bilayer constructs). The majority of available products are acellular dermal substitutes derived from placental membranes or animal tissue (Snyder, 2020).

Clinical variables influencing product selection include wound etiology, size, depth, duration, vascular status, and infection control. Appropriate use requires documented failure of prior standard care (typically 4 weeks), adequate site preparation (debridement), and ongoing adjunctive care (offloading for diabetic foot ulcers, compression for venous leg ulcers). Regulatory pathways vary; products may be regulated as medical devices (Premarket Approval or 510(k) clearance) or as Human Cells, Tissues, and Cellular or Tissue-based Products (HCT/Ps) (Vecin, 2023).

Findings

Guidelines and evidence reviews agree that skin substitutes are adjuncts to optimized standard care, adequate perfusion, and infection control, with escalation typically occurring when ≥50% area reduction is not achieved by 4 weeks, and with one product used at a time. For diabetic foot ulcers, meta-analyses and society guidelines indicate higher complete-closure rates compared to standard care when used in conjunction with effective offloading and after infection is treated, with safety profiles similar to those of standard care. For venous leg ulcers and nonhealing dermal wounds, systematic reviews report an adjunctive benefit when paired with sustained compression and objective monitoring. However, the effects are heterogeneous and influenced by the chronicity of the ulcer. In acute thermal burns, randomized trials and meta-analyses support the selective use of these matrices for temporary coverage and donor-site sparing, with improved scar outcomes, but slower early epithelialization for some matrices. In contrast, guidelines do not support routine use for pressure ulcers due to limited evidence.

Guidelines

Chronic wound management aims to restore cutaneous structural and functional integrity (Agency for Healthcare Research and Quality [Snyder, 2020]). Yet, chronic wounds frequently stall in the inflammatory phase, representing a failure in the normal healing sequence (Wound Healing Foundation [Eriksson, 2022]). Professional guidelines establish a hierarchical approach, reserving advanced therapies, such as skin

substitutes, for wounds that fail to respond despite optimized local wound environments. The Wound Healing Foundation [Eriksson, 2022] emphasizes that advanced modalities require meticulous wound bed preparation through thorough debridement of nonviable tissue and biofilm (Wounds International Consensus Document on the Use of Wound Antiseptics in Practice [Nair, 2023]), with the International Working Group on the Diabetic Foot [Schaper, 2023] advising that skin substitutes be deferred until infection, including osteomyelitis, is controlled; offloading should continue during infection management.

Professional societies define treatment escalation using objective metrics: failure to achieve a 50% reduction in wound area after 4 weeks of optimized, etiology-specific standard care predicts long-term non-healing and justifies consideration of advanced therapy (Wound Healing Foundation [Eriksson, 2022]; Agency for Healthcare Research and Quality [Snyder, 2020]). This temporal benchmark, validated across multiple guidelines, signals when adjunctive interventions become appropriate. Randomized controlled trials do not support the routine use of biologically active products as first-line treatment for diabetic foot ulcers; their use is applicable only after documented failure of optimized care with confirmed healing potential (International Working Group on the Diabetic Foot [Chen, 2023]). Guidelines recommend using one adjunct at a time, as efficacy trials evaluate products individually against optimized care (Agency for Healthcare Research and Quality [Snyder, 2020]).

Adequate tissue perfusion remains fundamental to healing potential, necessitating rigorous vascular assessment before initiating advanced therapies (Wound Healing Foundation [Eriksson, 2022]). Because ankle–brachial index can be unreliable in diabetes, confirm distal perfusion: toe pressure ≥30 mmHg or $TcPO_2$ ≥25 mmHg indicate adequate healing potential, with values below prompting urgent imaging and revascularization (International Working Group on the Diabetic Foot [Fitridge, 2023]); where available, skin perfusion pressure ≥40 mmHg also supports healing potential (Wound, Ostomy and Continence Nurses Society [Bonham, 2022]).

Advanced therapies cannot compensate for unaddressed underlying wound etiology. For neuropathic diabetic foot ulcers, effective mechanical offloading is foundational (International Working Group on the Diabetic Foot [Bus, 2024; Schaper, 2024]); for venous leg ulcers, sustained therapeutic compression is a prerequisite and must continue throughout treatment (Wound Healing Society [Marston, 2016]; Wound, Ostomy and Continence Nurses Society [Bonham, 2022]). Non-adherence to these etiology-specific measures renders advanced modalities inappropriate (International Working Group on the Diabetic Foot [Schaper, 2024]; Wound Healing Society [Marston, 2016]). The Wound Healing Society's 2023 update [Lavery, 2024] reinforces this hierarchy, maintaining Level I evidence for certain cellular and acellular matrices in chronic diabetic foot ulcers that are unresponsive to standard therapy, while emphasizing the use of single products with continued objective monitoring for early non-response.

Evidence strength varies by wound type. For pressure ulcers, the Wound Healing Society [Gould, 2024] does not recommend routine use of skin substitutes, given limited and inconsistent evidence. Conversely, cellular and acellular matrices may be considered for diabetic foot or venous leg ulcers failing optimized standard care (lacking ≥50% area reduction at four weeks) when perfusion is adequate and infection controlled (Agency for Healthcare Research and Quality [Snyder, 2020]; International Working Group on the Diabetic Foot [Schaper, 2024]). The application is not indefinite; failure to demonstrate significant progress within the initial weeks necessitates discontinuation of the product and a reassessment of the strategy (Wound Healing Foundation [Eriksson, 2022]). Across all indications, guidelines converge on foundational requirements: adequate perfusion, infection control, and optimized standard care must precede any advanced intervention.

Evidence review

Efficacy in wound closure and healing kinetics

Skin substitutes significantly enhance the probability of complete healing in chronic non-pressure wounds compared to standard care; however, their impact on healing velocity in acute burns is more variable, depending on the material and wound depth. In the management of diabetic foot ulcers, a meta-analysis across twenty-nine randomized controlled trials (n = 3,109) demonstrated improved complete healing, yielding a pooled odds ratio of 2.9 versus standard care; this effect was robust, showing no modification by baseline age or wound size, and remained consistent (odds ratio 2.7) after correction for publication bias (Lu, 2025). Convergent evidence from a broad review of twenty-two randomized controlled trials (n = 1,668 participants with reported enrollment) spanning diabetic foot ulcers, venous leg ulcers, and pressure ulcers confirmed higher closure rates and shorter time to closure when utilizing advanced biologics such as amniotic membranes, dermal matrices, and bilayer collagen templates compared to standard care (Snyder, 2020). While effects in venous leg ulcers were directionally similar, the results exhibited greater heterogeneity, with benefits appearing more concentrated in ulcers of shorter duration (Snyder, 2020).

In the context of acute burns, the impact of acellular dermal substitutes on wound healing kinetics demonstrates adequate incorporation but often delayed initial epithelialization compared to standard autografting. A meta-analysis indicated that collagen-elastin matrices significantly delayed re-epithelialization at 4 to 7 days compared to split-thickness skin grafts alone (Mean Difference -7.30%; p = 0.02) (van den Bosch, 2024). This delay was accompanied by non-significant trends toward lower graft take (Mean Difference -3.13%) and increased need for regrafting (Odds Ratio 1.99) (van den Bosch, 2024). For acute full-thickness burns treated with bilayer dermal regenerative matrices (n = 800), the mean template take was 86%, necessitating subsequent grafting at an average of 24.2 days (Hicks, 2019). An exception involves specific xenografts in partial-thickness burns; compared to silver sulfadiazine (n = 115), acellular fish skin reduced the mean re-epithelialization time (9.7 versus 10.2 days) (El Araby, 2025).

Comparative effectiveness of cellular versus acellular substitutes

The comparative effectiveness between cellular and acellular products does not reveal a uniform advantage for either category across wound types, suggesting that efficacy is context-dependent. In the management of chronic wounds, six head-to-head randomized comparisons (n ≥ 436 across trials with reported enrollment) illustrated varied outcomes (Snyder, 2020). For instance, an acellular urinary bladder matrix demonstrated comparable results to a cellular dermal substitute in terms of closure rates, time to closure, and six-month recurrence rates (Snyder, 2020). In another comparison, a dehydrated amniotic and chorion membrane (acellular) outperformed a living bilayer construct (cellular) for twelve-week closure while requiring fewer graft applications (Snyder, 2020). Comparisons between two different cellular products were broadly similar, noting only a small-wound subgroup advantage for a cryopreserved placental membrane (Snyder, 2020). In the context of burns, cellular substitutes, such as Cultured Skin Substitutes, offer specific advantages in resource utilization by significantly reducing the requirement for donor skin harvesting through increased expansion ratios compared to meshed autografts (ratio 67 versus 4; $p<0.01$); however, this benefit is balanced against increased graft loss observed between postoperative days 7 and 14 ($p<0.05$) (Putri, 2024).

Long-term scar quality and functional outcomes

The application of dermal substitutes consistently demonstrates improvements in long-term scar quality and function following burn injury and reconstruction. Following acute burn injury, a meta-analysis comparing acellular dermal matrices with split-thickness skin grafts alone revealed a statistically significant improvement in

Vancouver Scar Scale scores at 6 months (Mean Difference -1.95; $p < 0.01$) (van den Bosch, 2024). This finding aligns with results from three randomized controlled trials (n=128), which also demonstrated a significant improvement in Vancouver Scar Scale scores when comparing combined skin substitutes and skin grafts to skin grafts alone (Standardized Mean Difference 1.38; 95% Confidence Interval 0.13–2.63; p=0.03) (Putri, 2024). The mean postoperative Vancouver Scar Scale score following acute burn treatment with dermal regenerative matrices was reported as 2.3 (Hicks, 2019). While objective elasticity measurements (Uf-ratio) for collagen-elastin matrices did not show statistically significant improvements over split-thickness skin grafts alone at 12 months (Mean Difference -0.05), subjective reports frequently noted enhanced pliability (van den Bosch, 2024; Putri, 2024).

Dermal substitutes are also utilized in burn scar reconstruction (n = 284) to address contractures, particularly in functional areas such as the neck, hand/wrist, and axilla (Hicks, 2019). Functional outcomes following reconstructive surgery are favorable; across four studies (n = 42), 95% of patients demonstrated objective improvements in range of motion following contracture release utilizing dermal regenerative matrices (Hicks, 2019). In these reconstructive settings, graft incorporation was higher than in acute applications (mean template take 95%; subsequent graft take 93%) (Hicks, 2019). However, quantitative outcomes regarding scar contraction reveal differences between materials; a comparison showed that collagen-elastin matrices resulted in statistically significantly higher contraction compared to bilayer collagen-glycosaminoglycan matrices (Mean Difference +25.21%; $p = 0.0003$), although this finding was confounded by heterogeneity in surgical application techniques (van den Bosch, 2024).

Safety profiles and patient experience

The safety profiles of skin substitutes are generally comparable to those of standard care across various wound etiologies. However, complication rates vary by material and clinical context, with certain materials offering advantages in terms of patient comfort and resource utilization. In chronic wound management, adverse event profiles were similar between advanced biologics and standard care, with infection and cellulitis being the dominant complications (Snyder, 2020). In the acute burn setting, adverse events associated with dermal regenerative matrices were reported across 72 studies (n = 1084), occurring at an overall rate of 13% (Hicks, 2019). The most frequent complication was infection (4.6%), commonly caused by Staphylococcus aureus and Pseudomonas aeruginosa; other complications included graft loss, hematoma, and contracture (Hicks, 2019). Patient-reported outcomes indicate advantages for specific materials in partial-thickness burns; acellular fish skin grafts were associated with significant reductions in pain compared to silver sulfadiazine (Visual Analogue Scale 20.5 versus 29.2) and silver-impregnated dressings (Visual Analogue Scale 13.96 versus 24.79) (El Araby, 2025). Furthermore, fish skin significantly decreased the number of dressing changes required (1.6 versus 4.9) compared to silver sulfadiazine (El Araby, 2025).

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On 10/15/2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Service Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were *skin substitutes, dermal substitutes, cellular skin substitute.* We included the best available evidence, as per established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available), and professional guidelines informed by such evidence and clinical expertise.

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Policy updates

10/1/2025 initial review date and clinical policy effective date: 11/1/2025

11/2025: Policy created.

Appendix: product selection, details, and regulatory information

1. Purpose

This appendix provides a regulatory-verified framework to guide appropriate selection and continuation of advanced wound products for diabetic foot ulcers, venous leg ulcers, and thermal burns. It aligns product use with United States Food and Drug Administration labeling and establishes consistent decision rules for payer coverage determinations.

2. Scope

- Populations: Adults and children as permitted by Food and Drug Administration labeling for each product.
- Wound types:
  - Chronic ulcers: Diabetic foot ulcers and venous leg ulcers without exposed tendon, muscle, joint capsule, or bone (unless labeling explicitly permits).
  - Thermal burns: Partial-thickness, deep partial-thickness requiring surgery, full-thickness, and extensive burns as defined by Food and Drug Administration labeling.
- Required foundational care:

- Diabetic foot ulcer: Evidence-based offloading and infection control.
- Venous leg ulcer: Sustained therapeutic compression.
- All: Adequate perfusion, debridement as needed, moisture balance, and infection management.

3. Core Decision Principles

1. Food and Drug Administration Alignment First: Product selection must match the exact Food and Drug Administration-labeled indication (etiology, depth, duration, anatomic limits, population).
2. Evidence Hierarchy: Prefer Food and Drug Administration Premarket Approval, Biologics License Application, or Humanitarian Device Exemption products (Tier 1) when clinically appropriate; use 510(k) devices (Tier 2) when no Tier 1 option fits; reserve Human Cells, Tissues, and Cellular and Tissue-based Products (Tier 3) as the lowest tier, noting they are not Food and Drug Administration-approved for wound indications.
3. Clinical Eligibility Gate: Diabetic foot ulcers and venous leg ulcers must have documented failure of optimized standard care at four weeks unless a Food and Drug Administration label requires a longer minimum duration.
4. Four-Week Reassessment Rule: Continue a product beyond four weeks only if the wound area has decreased by at least 50%; otherwise, stop, reassess, and consider an alternative class.

4. Regulatory Tier Definitions:

- Tier 1 (Premarket Approval / Biologics License Application / Humanitarian Device Exemption): Food and Drug Administration-approved (Premarket Approval), licensed (Biologics License Application), or authorized (Humanitarian Device Exemption) products with labeled wound indications.
- Tier 2 (510(k)): Devices cleared for wound management indications (based on substantial equivalence).
- Tier 3 (Human Cells, Tissues, and Cellular and Tissue-based Products): Human cells/tissues regulated solely under section 361; no Food and Drug Administration wound-etiology approval.

Product and evidence summary table

Product	Pathway / Tier	Food and Drug Administration Identifier	Labeled Indication	Systematic Review	Key Guideline	Key Evidence (Author, Year)	Evidence Strength
Diabetic Foot Ulcers							
Apligraf (diabetic foot ulcer)	Premarket Approval / Tier 1	P950032/S016 (May 22, 1998)	“Full-thickness neuropathic diabetic foot ulcers at least 3 weeks that	Santema, 2016	Hingorani, 2016	Veves, 2001	A

			extend through the dermis, without tendon, muscle, capsule, or bone exposure; with standard care."				
Dermagraft (diabetic foot ulcer)	Premarket Approval / Tier 1	P000036 (Sep 28, 2001)	"Full-thickness diabetic foot ulcers at least 6 weeks that extend through the dermis, without tendon, muscle, joint capsule, or bone exposure; in patients with adequate blood supply."	Santema, 2016	Hingorani, 2016	Marston, 2003	B
Omnigraft (diabetic foot ulcer)	Premarket Approval / Tier 1	P900033/S042 (Jan 7, 2016)	"Partial- and full-thickness neuropathic diabetic foot ulcers greater than 6 weeks, with no capsule, tendon, or	Sui, 2024	Hingorani, 2016	Driver, 2015	B

			bone exposed, when used in conjunction with standard diabetic ulcer care."				
OASIS Matrix	510(k) / Tier 2	K061711 (Jul 19, 2006)	"Management of wounds including: partial and full-thickness wounds; pressure ulcers; venous ulcers; diabetic ulcers." (device-cleared for wound management, not etiology-specific approval)	None found as of Nov 2025	Hingorani, 2016	None found as of Nov 2025	C
PriMatrix	510(k) / Tier 2	K083440 (Dec 12, 2008)	"Management of wounds… partial and full thickness… pressure, diabetic, and venous ulcers; second-degree burns."	None found as of Nov 2025	—	Kavros, 2014 (Prospective cohort)	C

			(device-cleared for wound management, not etiology-specific approval)				
Kerecis (fish-skin)	510(k) / Tier 2	K132343 (Oct 23, 2013); K190528	“Treating partial- and full-thickness wounds, ulcers, and draining, surgical, and traumatic wounds.” (device-cleared for wound management, not diabetic foot ulcer-specific approval)	Ruiz-Muñoz, 2024	—	Dardari, 2024	B
EpiFix	361 Human Cells, Tissues, and Cellular and Tissue-based Products / Tier 3	—	Not Food and Drug Administration-approved for wound indications.	Haugh, 2017	—	Zelen, 2013. Evidence base consists of small randomized controlled trials with sponsorship; heterogeneity and risk-of-bias persist.	B
Grafix	361 Human Cells, Tissues,	—	Not Food and Drug Administration-	None found as of Nov 2025	—	Lavery, 2014. Evidence from small	B

	and Cellular and Tissue-based Products / Tier 3		approved for wound indications.			randomized controlled trial; industry sponsorship noted.	
DermACELL	361 Human Cells, Tissues, and Cellular and Tissue-based Products / Tier 3	—	Not Food and Drug Administration-approved for wound indications.	Sui, 2024	—	Walters, 2016. Evidence is largely nonrandomized.	C
Venous Leg Ulcers							
Apligraf (venous leg ulcer)	Premarket Approval / Tier 1	P950032 (May 22, 1998)	“Non-infected partial and full-thickness skin ulcers due to venous insufficiency greater than 1 month that extend through the dermis, without tendon, muscle, capsule, or bone exposure; with compression.”	Jones, 2013	O’Donnell, 2014	Falanga, 1998	A

OASIS Matrix	510(k) / Tier 2	K061711 (Jul 19, 2006)	“Management of wounds including: partial and full-thickness wounds; pressure ulcers; venous ulcers; diabetic ulcers.” (device-cleared for wound management, not etiology-specific approval)	Jones, 2013	O’Donnell, 2014	Mostow, 2005	A
EpiFix	361 Human Cells, Tissues, and Cellular and Tissue-based Products / Tier 3	—	Not Food and Drug Administration-approved for wound indications.	Haugh, 2017	—	Serena, 2014. Evidence base consists of small randomized controlled trials with sponsorship.	B
AmnioBand / Guardian	361 Human Cells, Tissues, and Cellular and Tissue-based Products / Tier 3	—	Not Food and Drug Administration-approved for wound indications.	None found as of Nov 2025	—	Serena, 2022. Evidence from multicenter randomized controlled trial; industry sponsorship noted.	B

Thermal Burns							
StrataGraft	Biologics License Application / Tier 1	STN 125730 (Jun 15, 2021)	“Treatment of adult patients with debrided thermal burns… intact dermal elements… for which surgical intervention is clinically indicated.”	None found as of Nov 2025	None found as of Nov 2025	Holmes, 2021	B
Integra Dermal Regeneration Template	Premarket Approval / Tier 1	P900033 (Jan 7, 2016)	“Postexcisional treatment of life-threatening full-thickness or deep partial-thickness thermal injuries… autograft not available or not desirable.”	None found as of Nov 2025	None found as of Nov 2025	Heimbach, 2003	C
TransCyte	Premarket Approval / Tier 1	P960007 (Mar 18, 1997)	“Temporary wound covering for surgically excised full-thickness and deep partial-thickness thermal	None found as of Nov 2025	None found as of Nov 2025	Kumar, 2004	B

			burns prior to autograft; and mid-dermal to indeterminate depth burns expected to heal without autografting.”				
RECELL Autologous Cell Harvesting Device	Premarket Approval / Tier 1	BP170122 (Sep 20, 2018)	“Treatment of thermal burn wounds and full-thickness skin defects; for direct application to acute partial-thickness thermal burns in adults aged at least 18 years; or with meshed autograft for acute full-thickness thermal burns in pediatric and adult patients and full-thickness skin defects in patients aged at	Daneshi, 2025 (conference abstract only)	None found as of Nov 2025	Holmes, 2018	B

			least 15 years."				
Epicel	Humanitarian Device Exemption / Tier 1	H990002 (Oct 25, 2007)	"Deep dermal or full thickness burns comprising … at least 30% Total Body Surface Area." Authorized under Humanitarian Device Exemption based on probable benefit, not demonstrated effectiveness.	None found as of Nov 2025	None found as of Nov 2025	Hickerson, 2019	B
Biobrane	510(k) / Tier 2	K242146 (Dec 17, 2024)	"Covering clean partial thickness burn wounds; Split thickness donor sites." (device-cleared for wound management, not etiology-specific approval)	Wasiak, 2013	None found as of Nov 2025	Kumar, 2004: pediatric partial-thickness burns; faster re-epithelialization vs silver sulfadiazine; comparator TransCyte arm reported.	B

Suprathel	510(k) / Tier 2	K090160 (May 20, 2009)	“Temporary coverage of non-infected skin defects, such as superficial wounds, under sterile conditions.” (device-cleared for wound management, not etiology-specific approval)	None found as of Nov 2025	None found as of Nov 2025	Hundeshagen, 2018	B

Quick-reference and policy rules

Wound-to-product mapping table

Wound Characteristic	Preferred Product Class	Regulatory Tier Notes
Small/superficial diabetic foot ulcer (no exposure)	Bilayer living cell construct (e.g., Apligraf)	Tier 1; diabetic foot ulcer at least 3 weeks.
Moderate diabetic foot ulcer (through dermis, no exposure)	Cellular dermal scaffold (e.g., Dermagraft)	Tier 1; diabetic foot ulcer at least 6 weeks.
Partial–full thickness diabetic foot ulcer needing scaffold (no exposure)	Dermal regeneration template (e.g., Omnigraft)	Tier 1; diabetic foot ulcer at least 6 weeks.
When Tier 1 is unsuitable (diabetic foot ulcer/venous leg ulcer)	Xenogenic/acellular matrices (e.g., OASIS, Kerecis)	Tier 2; cleared for wound management.
Venous leg ulcer (with sustained compression)	Bilayer living cell construct (e.g., Apligraf)	Tier 1; venous leg ulcer greater than 1 month.

Partial-thickness burns	Biosynthetic temporary covers (e.g., Biobrane; Suprathel)	Tier 2; partial-thickness/donor site coverage.
Deep partial-thickness burns needing surgery	Allogeneic cellular construct (StrataGraft)	Tier 1.
Full-thickness burns (bridge to autograft)	Temporary cover (TransCyte); dermal template (Integra)	Tier 1.
Extensive burns (at least 30% Total Body Surface Area)	Cultured autografts (Epicel)	Tier 1 (Humanitarian Device Exemption).
Autograft sparing/adjunct	Autologous cell harvesting (RECELL)	Tier 1.
Any ulcer with exposed tendon/bone/capsule	Not eligible for products above unless labeling explicitly permits.	Optimize surgical coverage first.

Chronicity thresholds table

Condition	Minimum Duration Before Advanced Therapy (per Food and Drug Administration Labeling)
Diabetic foot ulcer treated with Apligraf	at least 3 weeks
Diabetic foot ulcer treated with Dermagraft	at least 6 weeks
Diabetic foot ulcer treated with Omnigraft	at least 6 weeks
Venous leg ulcer treated with Apligraf	greater than 1 month (with compression)