PROVIDER*ALERT*

AmeriHealth Caritas Louisiana

To: **AmeriHealth Caritas Louisiana Providers**

Date: **September 15, 2026**

Subject: **Approved Clinical Policies**

Summary: **Six Approved Clinical Policies**

AmeriHealth Caritas Louisiana would like to inform you of the six clinical policies approved by the Louisiana Department of Health in accordance with La. R.S. 46:460.54. The guidelines are effective **October 15, 2026**, and will be located at the following link on our website under Clinical Policies:

https://www.amerihealthcaritasla.com/provider/resources/clinical-policies

1. Autologous Fat Grafting and Injectable Soft-Tissue Fillers
2. Balloon Spacer Devices for Management of Massive Rotator Cuff Tears
3. Skin Substitutes for Chronic Wounds
4. Transcatheter therapy for Severe Tricuspid Insufficiency
5. Transperineal Laser Ablation of the Prostate for Benign Prostatic Hyperplasia
6. ZOLL Heart Failure Management System

Reminder: If your practice is not registered with our website portal, NaviNet, we highly recommend registering. To register, please visit www.navinet.net to sign up or contact your Provider Account Executive for details.

Questions:
Thank you for your continued support and commitment to the care of our members. If you have questions about this communication, please contact AmeriHealth Caritas Louisiana's Provider Services department at 1-888-922-0007 or your Provider Network Management Account Executive.

Missed an alert?
You can always find a complete listing of provider alerts on the Newsletters and Updates page of our website.

Need to update your provider information? Send full details to network@amerihealthcaritasla.com

Autologous Fat Grafting and Injectable Soft-Tissue Fillers

Clinical Policy ID: CCP.1550

Recent review date: 9/30/2025

Next review date: 1/31/2027

Policy contains: autologous fat grafting, injectable fillers, breast reconstruction, systemic sclerosis, digital ulcers, chronic wounds, scar fibrosis, burn scars, fistula management, injection laryngoplasty, vocal fold paralysis, hyaluronic acid, poly-L-lactic acid, calcium hydroxylapatite, collagen, HIV-associated lipoatrophy

Coverage policy

Autologous fat grafting and injectable soft-tissue fillers (e.g., collagen, Sculptra, Radiesse) are clinically proven and, therefore, may be medically necessary for the following indications:

Autologous fat grafting:

- Correcting contour irregularities and improving tissue quality after radiotherapy in post-mastectomy breast reconstruction (Zhong, 2025)
- Adjunctively treating systemic sclerosis digital ulcers to promote healing when combined with systemic therapy (Campochiaro, 2025; Suliman, 2023)

Injectable soft-tissue fillers:

- Restoring facial volume in human immunodeficiency virus-associated facial lipoatrophy with agents recognized by the Food and Drug Administration (e.g., poly-L-lactic acid, calcium hydroxylapatite), improving volume and quality-of-life outcomes (Jagdeo, 2015)

Additional uses for autologous fat grafting and injectable soft-tissues for vocal cord paralysis or glottic insufficiency are outlined in CCP.1157 Supraglottoplasty and laryngoplasty. All other uses of autologous fat grafting and injectable soft-tissue are considered investigational/not clinically proven and, therefore, not medically necessary. These include, but are not limited to:

- Using autologous fat grafting for generalized chronic wound management outside of systemic sclerosis digital ulcers; current evidence for generalized wounds is heterogeneous and characterized by very low certainty (Malik, 2020).
- Using injectable soft-tissue fillers for acne scar management, as the supporting evidence is characterized by heterogeneity and low quality (Albargawi, 2025).
- Using autologous fat grafting or injectable soft-tissue fillers for general aesthetic enhancement or to alter normal anatomic variation related to aging (cosmetic use).

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Implant or flap revision
- Capsulotomy/capsulectomy
- Local wound care
- Digital sympathectomy
- Revascularization procedures

Background

Autologous fat grafting is a surgical procedure involving the transplantation of an individual's own adipose tissue from one anatomical site to another for reconstructive or therapeutic purposes. The procedure involves harvesting adipose tissue via liposuction, processing the lipoaspirate using minimally manipulative techniques (e.g., centrifugation, filtration), and injecting the processed fat into the target area (Haddad, 2021). The mechanisms of action involve both structural replacement , restoring bulk in areas of volume loss (Lakhani, 2012) and regenerative effects, including the modulation of inflammation, promotion of angiogenesis, and remodeling of scar matrix (Schipper, 2024; Arena, 2025; Xiao, 2024). This policy addresses minimally manipulated autologous fat grafting, excluding enriched products such as stromal vascular fraction or nanofat.

Injectable soft tissue fillers are substances injected into the dermal or subcutaneous tissue. Common materials include hyaluronic acid, calcium hydroxylapatite, poly-L-lactic acid, and collagen. These agents serve as either physical fillers, providing immediate volume restoration (e.g., hyaluronic acid), or bio-stimulatory fillers, which stimulate natural collagen production (neocollagenesis) over time (e.g., poly-L-lactic acid, calcium hydroxylapatite) (Albargawi, 2025; Jagdeo, 2015).

While widely utilized for cosmetic enhancement (Amiri, 2024), both autologous fat grafting and injectable fillers are applied across diverse noncosmetic therapeutic and reconstructive indications. In reconstructive contexts, autologous fat grafting is used in post-mastectomy breast reconstruction to manage contour irregularities and address tissue damage from radiotherapy (Zhong, 2025). Fillers such as poly-L-lactic acid and calcium hydroxylapatite are employed to treat human immunodeficiency virus-associated facial lipoatrophy, restoring facial volume loss related to antiretroviral therapy to reduce social stigma and improve quality of life (Jagdeo, 2015). Furthermore, autologous fat grafting has applications in tissue regeneration for the management of systemic sclerosis digital ulcers, chronic wounds, and burn scars (Campochiaro, 2025; Xiao, 2024; Lesmanawati, 2024).

Findings

Across noncosmetic indications, findings diverge by modality. Autologous fat transfer is endorsed for breast reconstruction and appears oncologically safe; in systemic sclerosis it improves short-term digital-ulcer healing, while effects on hand function and facial fibrosis are inconsistent and of lower certainty. Evidence for chronic wounds, scar fibrosis, and fistula care is low to very low, because studies are small and heterogeneous, and variable resorption limits durability. Injectable soft-tissue restore facial volume in human immunodeficiency virus–associated lipoatrophy, with hyaluronic acid safer but shorter-lived, poly-L-lactic acid longer-lasting but with more nodules, and calcium hydroxylapatite intermediate. Randomized trials remain scarce and technique variability limits generalizability, so conclusions distinguish guideline-supported practice from areas that remain investigational.

Guidelines

Autologous fat grafting in breast reconstruction

Society guidelines endorse autologous fat grafting as a reconstructive adjunct after oncologic breast surgery for contour correction, implant rippling, and irradiated skin improvement (Zhong 2025; American Society of Plastic Surgeons 2015). Ontario Health recommends fat grafting for these indications, citing improved patient-reported outcomes and no increased cancer recurrence based on a systematic review utilizing rigorous methodology, including the Appraisal of Guidelines for Research & Evaluation II framework (Zhong 2025). The American Society of Plastic Surgeons assigns a grade B recommendation based on consistent case-series evidence. They characterize the procedure as reconstructive, note its use for postmastectomy pain, and link coverage to the Women's Health and Cancer Rights Act while acknowledging insurer denials (American Society of Plastic Surgeons 2015).

Autologous fat grafting for systemic sclerosis

For digital ulcers in systemic sclerosis, the World Scleroderma Foundation conditionally advises autologous adipose tissue grafting as an adjunct to systemic therapy. This recommendation (evidence level three, expert opinion) is based on one randomized, controlled trial and cohort studies showing improved healing. The methodology included systematic reviews, Cochrane reviews, and the ROBINS-I (risk of bias in non-randomized studies of interventions) tool, and consensus procedures (Campochiaro 2025). The committee noted that other injectables, such as botulinum toxin for refractory ulcers, are supported mainly by observational data, highlighting evidence quality gaps that limit the strength of recommendations for those alternatives (Campochiaro 2025).

Systematic reviews and meta-analyses for autologous fat grafting

Breast reconstruction and oncologic safety

A large meta-analysis of 22 cohort studies (n = 9,971) provides moderate-certainty evidence regarding the oncologic safety of autologous fat grafting in individuals undergoing breast reconstruction after cancer treatment. The analysis found no increase in local recurrence, regional recurrence, distant metastasis, or mortality associated with fat grafting compared with controls (Tian, 2022). These findings establish the safety of the procedure in this specific oncologic population, supporting its use for reconstructive indications (Tian, 2022).

Systemic sclerosis

Autologous fat grafting is effective for digital ulcer healing in systemic sclerosis, although evidence is less robust for improving hand function or facial fibrosis. Multiple systematic reviews, 13 studies (n = 170) and 29 studies (n = 704), synthesizing data from prospective cohorts and one randomized, sham-controlled trial reported high healing proportions and superiority of grafting over sham injection at eight weeks, supporting moderate certainty for short-term healing (Suliman, 2023); (Perrier, 2025). Regarding hand function and ischemic symptoms, reviews, 29 studies (n = 704), reported signals of reduced ischemic hand pain, but effects on mobility, grip measures, or range of motion were inconsistent, resulting in low certainty (Perrier, 2025). For facial fibrosis, improvements in mouth opening, mouth handicap scores, and subjective skin pliability were reported, but objective fibrosis measures were inconsistent, and the durability of effects remains uncertain due to variable graft resorption (Schipper, 2024).

Chronic wounds

The evidence regarding autologous fat grafting for generalized chronic wounds is characterized by significant heterogeneity and very low certainty, which is insufficient to establish the procedure as the standard of care. One systematic review of 10 observational studies (n = 389) analyzed various fat therapy techniques, attributing the very low certainty of evidence to the lack of controls, inconsistent reporting, and substantial procedural variations, despite noting a favorable safety profile (Malik, 2020). A separate meta-analysis of 21 randomized controlled trials (n = 1,119) suggested that human fat products, including minimally manipulated autologous fat grafting, accelerated wound healing rates, shortened time to complete healing, and reduced pain compared to conventional treatment (Xiao, 2024). However, the applicability of these findings to generalized chronic wound care remains limited by the very low certainty and heterogeneity noted across the broader literature.

Vocal fold insufficiency

Evidence regarding the efficacy of autologous fat grafting for vocal fold insufficiency is of very low certainty, primarily due to unpredictable graft durability and resorption. A Cochrane systematic review determined that no methodologically sound randomized controlled trials were available to compare the efficacy of autologous fat with other injectable materials for unilateral vocal fold paralysis (Lakhani, 2012). While systematic reviews of observational studies, 13 studies (n = 472), suggest short- to medium-term improvements, these studies are subject to significant bias, lack control groups, and frequently show a decline in effect requiring reintervention (Campagnolo, 2023). A meta-analysis of 49 observational studies (n = 1,166) found statistically significant short-term improvements in the Voice Handicap Index, clinician-rated perceptual voice analyses, maximum phonation time, and acoustic parameters at six months (Haddad, 2021). The analysis found no significant difference in outcomes based on the use of liposuction or incision as the harvest technique (Haddad, 2021).

Scar fibrosis and burns

Systematic reviews examining autologous fat grafting for scar fibrosis suggest potential improvements in appearance but limited functional benefits, resulting in low certainty evidence. For chronic burn scars, synthesized evidence from six studies (n = 241) indicates improvements in clinician-rated scar scales and histologic architecture when injected fat grafting is used, particularly when combined with fractional laser for facial scars (Lesmanawati, 2024). Symptomatically, higher satisfaction and some improvements in hand movement were reported in six studies (n = 241), but effects on function, pain, or itch were mixed (Lesmanawati, 2024). Divergent findings were noted in pediatric populations within a synthesis of six studies (n = 241), where one randomized trial found no improvement compared to saline (Lesmanawati, 2024). Evidence for acute burns was confounded by the use of topical nanofat, which is outside the scope of minimally manipulated grafting (Lesmanawati, 2024).

Fistula management

The available systematic reviews provide insufficient evidence regarding the efficacy of minimally manipulated autologous fat grafting for fistula management. Reviews addressing perianal Crohn's fistulas and nonenteric cutaneous fistulas, four studies (n = 49) and seven studies (n = 13) respectively, predominantly synthesized studies that utilized techniques involving more than minimal manipulation, such as microfragmented fat or stromal vascular fraction (De Gregorio, 2023; Bonomi, 2025). Furthermore, in four studies (n = 49), the frequent use of concomitant surgical maneuvers confounds the attribution of effects (De Gregorio, 2023). Consequently, these reviews do not permit conclusions specific to minimally manipulated autologous fat grafting for these indications.

Systematic reviews and meta-analyses for injectable soft-tissue fillers

Vocal fold insufficiency (injection laryngoplasty)

Injectable soft tissue fillers consistently provide measurable functional gains in the treatment of unilateral vocal fold paralysis. A meta-analysis of 32 studies (n = 1,917) showed short- to medium-term improvement in patient-reported quality of life, maximal phonation time, and normalized glottal gap, with adverse events rare and transient (Alkhalifah, 2025). A broader meta-analysis of 82 studies reported a mean maximal phonation time gain of 4.71 seconds (postop: n = 1,781; pre n = 1,981), along with significant reductions in jitter and shimmer (Safia, 2024).

The timing of intervention and the material used are major predictors of benefit (Safia, 2024). Early injection laryngoplasty, six months or less, reduced the relative risk of subsequent permanent thyroplasty to 0.25 across 275 pooled cases, with mean injection time 4.5 months (Vila, 2018; Safia, 2024). Reviews focused on hyaluronic acid confirm durability clustered at six to 12 months with inflammatory complications in 1.47% of 476 treated individuals (Švejdová, 2022). Comparative studies reinforce clinical effectiveness relative to alternatives; 17 head-to-head studies showed no consistent superiority of injection laryngoplasty versus thyroplasty, arytenoid adduction, or reinnervation across perceptual, acoustic, or laryngoscopic outcomes (Siu, 2016; Safia, 2024).

Human immunodeficiency virus-associated facial lipoatrophy

Injectable soft tissue fillers demonstrate consistent safety, efficacy, and durability for restoring facial volume in human immunodeficiency virus-associated facial lipoatrophy. Multiple fillers improve contour and quality of life

but differ in durability and complication profiles (Jagdeo, 2015). Six observational studies of hyaluronic acid showed consistent volume restoration at six and 12 months, offering a safe, reversible option for short- to medium-term use (Jagdeo, 2015).

Longer-lasting fillers extend benefit but may increase complication rates. Poly-L-lactic acid, supported by three randomized trials and 20 observational studies, provides more durable correction, sustaining tissue depth gains at 48 weeks in randomized cohorts (n = 130), but carried a higher risk of nodule formation (Jagdeo, 2015). Calcium hydroxylapatite also offers predictable medium-term benefit (Jagdeo, 2015). In contrast, polyalkylimide gel demonstrated high infectious complication rates, 3.3% to 19%, in long-term observational series (Jagdeo, 2015).

References

On 9/8/2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were Autologous fat grafting, fat transfer, lipofilling, adipose tissue graft, dermal fillers, injectable fillers, soft tissue fillers, hyaluronic acid, poly-L-lactic acid, calcium hydroxylapatite, collagen injection. We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Albargawi S. Synthetic dermal fillers in treating acne scars: a comparative systematic review. *J Cosmet Dermatol*. 2025;24(1):e16752. Doi:10.1111/jocd.16752.

Alkhalifah KM, Ahmed W, Alnawmasi HS, et al. The use of hyaluronic acid in the treatment of unilateral vocal fold paralysis: a systematic review and meta-analysis. *Cureus*. 2025;17(6):e85728. Doi:10.7759/cureus.85728.

American Society of Plastic Surgeons. Post-mastectomy fat graft/fat transfer: guiding principles. Published October 2015. Accessed September 14, 2025. https://www.plasticsurgery.org/documents/Health-Policy/Principles/principle-2015-post-mastectomy-fat-grafting.pdf

Amiri M, Meçani R, Llanaj E, et al. Calcium hydroxylapatite (CaHA) and aesthetic outcomes: a systematic review of controlled clinical trials. *J Clin Med*. 2024;13(6):1686. Doi:10.3390/jcm13061686.

Arena A, Troise S, De Francesco F, et al. Fat graft as regenerative treatment of facial manifestations of systemic sclerosis: a systematic review on the role of adipose tissue-derived stem cells and on surgical outcomes to define a new standardized injection protocol. *Wound Repair Regen*. 2025;33(3):e70045. Doi: 10.1111/wrr.70045.

Bonomi F, Limido E, Harder Y, Galetti K, De Monti M. Autologous fat grafting for the treatment of non-enteric cutaneous fistulas: a systematic literature review. *Surg Tech Dev*. 2025;14(3):26. Doi:10.3390/std14030026.

Campagnolo AM, Priston J, Nickel V, Benninger M. Vocal fold fat injection for glottic insufficiency: a systematic review. *J Voice*. 2023 S0892–1997(23)00304–1(online ahead of print). Doi:10.1016/j.jvoice.2023.09.029.

Campochiaro C, Suliman YA, Giuggioli D, et al. Recommendations for the local management of digital ulcers in systemic sclerosis: a report from the World Scleroderma Foundation (WSF) 'Ad hoc committee'. *J Scleroderma Relat Disord*. 2025 (published online May 15, 2025). Doi:10.1177/23971983251339821.

De Gregorio M, Tiang T, Lee T, et al. Autologous fat graft injections for the treatment of perianal fistulas in Crohn's disease: a systematic review and single-arm meta-analysis. *ANZ J Surg*. 2023;93(5):1162–1168. Doi:10.1111/ans.18231.

Jagdeo J, Ho D, Lo A, Carruthers A. A systematic review of filler agents for aesthetic treatment of HIV facial lipoatrophy (FLA). *J Am Acad Dermatol*. 2015;73(6):1040–1054.e14. Doi:10.1016/j.jaad.2015.08.040.

Lakhani R, Fishman JM, Bleach N, Costello D, Birchall M. Alternative injectable materials for vocal fold medialisation in unilateral vocal fold paralysis. *Cochrane Database Syst Rev*. 2012;10(10):CD009239. Doi:10.1002/14651858.CD009239.pub2.

Lesmanawati FE, Windura CA, Saputro ID, Hariani L. Autologous fat grafting and adipose-derived stem cells therapy for acute burns and burn-related scar: a systematic review. *Tzu Chi Med J*. 2024;36(2):203–211. Doi:10.4103/tcmj.tcmj_189_23.

Malik D, Luck J, Smith OJ, Mosahebi A. A systematic review of autologous fat grafting in the treatment of acute and chronic cutaneous wounds. *Plast Reconstr Surg Glob Open*. 2020;8(5):e2835. Doi:10.1097/GOX.0000000000002835.

Perrier A, Pugnet G, Chaput B, Gandolfi S. Hand surgical and injectable treatments in systemic sclerosis: a systematic review of published cases. *J Scleroderma Relat Disord*. 2025 (published online Jun 17, 2025). Doi:10.1177/23971983251348059.

Schipper JAM, Verhoef LL, Schepers RH, et al. Regenerative treatments for scleroderma of the face. *Clin Exp Rheumatol*. 2024;42(8):1675–1689. Doi:10.55563/clinexprheumatol/y2p4ib.

Suliman YA, Campochiaro C, Hughes M, et al. Surgical management of digital ulcers in systemic sclerosis: a systematic literature review. *Semin Arthritis Rheum*. 2023;63:152266. Doi:10.1016/j.semarthrit.2023.152266.

Tian D, Hu Z, Liu J, et al. The prognosis outcomes of autologous fat transfer for breast reconstruction after breast cancer surgery: a systematic review and meta-analysis of cohort studies. *Gland Surg*. 2022;11(3):386-397. Doi:10.21037/gs-22-297.

Xiao Y, Nie M, Xu W, Zhang J, Lei S, Wu D. The efficiency of human fat products in wound healing: a systematic review and meta-analysis. *Int Wound J*. 2024;21(9):e70016. Doi:10.1111/iwj.70016.

Zhong T, Fletcher GG, Brackstone M, et al. Postmastectomy breast reconstruction in patients with non-metastatic breast cancer: an Ontario Health (Cancer Care Ontario) clinical practice guideline. *Curr Oncol.* 2025;32(6):357. Doi:10.3390/curroncol32060357.

Policy updates

9/15/2025initial review date and clinical policy effective date: TBD

Balloon Spacer Devices for Management of Massive Rotator Cuff Tears

Clinical Policy ID: CCP. 1549

Recent review date: 9/30/2025

Next review date: 1/31/2027

Policy contains: subacromial balloon spacer, biodegradable balloon spacer, shoulder spacer, rotator cuff tear, massive irreparable rotator cuff tear, rotator cuff injuries.

Coverage policy

Subacromial balloon spacer implantation for the treatment of massive, irreparable rotator cuff tears is considered investigational/not clinically proven and therefore not medically necessary.

Background

Rotator cuff tears affect adults across their lifespan and become more common with age (Varacallo, 2024). Population studies that include people without symptoms estimate full-thickness tears in roughly 20% of adults (Yamamoto, 2010). Prevalence rises further with aging, with more than 50% of people in their 80s showing rotator cuff changes on imaging (Tempelhof, 1999). Many tears remain silent at first, which delays diagnosis and allows deterioration of tendon and muscle (Keener, 2015).

What defines a massive, irreparable rotator cuff tear? Clinicians use size and anatomy to define massive tears, which account for about 10% to 40% of diagnosed full-thickness tears (Agout, 2018). A tear larger than five centimeters or involving two or more cuff tendons qualifies as massive (Sánchez-Losilla, 2022). Tears that are considered irreparable show a 50% or more fatty change on magnetic resonance imaging, tendon retraction to the socket edge, or a space between the acromion and the ball of the upper arm bone of less than seven millimeters on radiographs (Sánchez-Losilla, 2022). These markers signal tissue that surgeons cannot mobilize back to bone with acceptable tension and that will not regain function after a standard repair (Virk, 2016).

Reverse total shoulder arthroplasty is the most common operation when shoulder function is lost and the cuff cannot be restored (Virk, 2016). Surgeons place the ball on the shoulder blade and the socket on the upper arm so the deltoid muscle can lift the arm in place of the torn cuff (Berliner, 2024). They select this option most often for older adults or for any individual with arthritis or pseudoparalysis who needs reliable pain relief and overhead use of the arm (Berliner, 2024). The tradeoff in reverse total should arthroplasty is the use of a prosthesis with long-term risks, so surgeons reserve it for individuals whose goals cannot be achieved with repair, partial repair, or tendon transfer (Virk, 2016).

For adults who prefer to preserve the native joint when repair is not feasible and arthroplasty is undesirable, surgeons may use a subacromial balloon spacer to restore spacing and improve mechanics (Sheean, 2024). This biodegradable implant sits between the acromion and the upper arm bone, helps recenter the ball, and reduces painful contact when the rotator cuff cannot stabilize the joint (Sheean, 2024). It dissolves over about one year and may be combined with other limited procedures to control pain and maintain motion (Sheean, 2024). In the United States, the Food and Drug Administration issued a De Novo classification in 2021 for a resorbable shoulder spacer for adults 65 years or older with massive, irreparable tears and mild to moderate arthritis, which guides labeling, testing, and use (Food and Drug Administration, 2021).

Findings

Evidence for biodegradable subacromial balloon spacers is mixed. Observational studies show that individuals who received these spacers experienced substantial improvements from baseline at 24 months: Constant-Murley scores increased from 34.8 to 67.9, visual analog pain scores decreased from 6.6 to 2.0, flexion improved from 108.5° to 151.2°, and approximately 83% achieved the minimal clinically important difference. However, comparative meta-analyses do not demonstrate superiority of the spacers over partial repair or arthroscopic debridement, with negligible effects on pain (mean difference −0.11) and motion. Randomized data are comparator dependent: adding a spacer to debridement yields worse function at 12 months and inferior 24-month quality of life, whereas outcomes are comparable to partial repair with shorter operative time and modest early advantages in elevation. Methodological limitations, heterogeneity, and sparse long-term threshold outcomes temper certainty. Guideline discordance mirrors these patterns, with the National Institute for Health and Care Excellence advising against routine use outside trials when debridement is suitable, and the American Academy of Orthopaedic Surgeons offering a consensus option for selected individuals without glenohumeral osteoarthritis.

Guidelines

Clinical practice guidelines present divergent recommendations regarding the use of biodegradable subacromial balloon spacers for the treatment of irreparable rotator cuff tears, reflecting the conflicting nature of the available evidence. The National Institute for Health and Care Excellence recommended against biodegradable

subacromial spacer use when arthroscopic debridement is suitable, and restricted use to research when debridement is not suitable. The committee based this chiefly on a U.K. multicenter randomized clinical trial in which debridement plus spacer was inferior to debridement alone at 12 months on Oxford Shoulder Score and Constant score, and the trial was stopped for futility. Evidence syntheses and a randomized clinical trial against partial repair show short- to mid-term improvements in pain and function within the group after spacer implantation, but long-term benefits remain uncertain (National Institute for Health and Care Excellence, 2023). Conversely, the American Academy of Orthopedic Surgeons states that balloon spacers may be considered for massive, irreparable rotator cuff tears without arthritis, but only as a consensus-based option — the lowest evidence grade — given inconsistent evidence and the need for individualized decision-making (American Academy of Orthopedic Surgeons, 2025). This consensus rating acknowledges the absence of reliable evidence due to significant heterogeneity and conflicting results among existing studies, including randomized trials that show both favorable and unfavorable outcomes for the device, depending on the comparator (American Academy of Orthopedic Surgeons, 2025).

Systematic reviews

Symptom and function improvement versus comparative advantage

Across the literature, balloon spacers have been shown to reliably produce within-group gains but not superiority over established options. Kunze synthesized contemporary reports and found high proportions of individuals achieving minimal clinically important difference on the Constant-Murley score (83%), American Shoulder and Elbow Surgeons score (83% – 87.5%), Oxford Shoulder Score (78% – 87%), and numeric pain rating scale (69% – 74%) from a pooled cohort (n = 748; spacer subset n = 379). However, achievement of a patient-acceptable symptom state and substantial clinical benefit was inconsistent and methodologically heterogeneous, limiting the ability to infer absolute outcome levels and durability of balloon spacers (Kunze, 2023).

In a head-to-head pooled comparison, Sandler reported greater visual analog scale pain reduction with debridement (adjusted mean difference −0.7, $P < 0.001$) and larger Constant-Murley gains (+5.5, $P < 0.001$), with neither study arm meeting the patient-acceptable symptom state threshold for pain (Sandler, 2024). The randomized evidence aligns with other researchers' findings. Metcalfe found Oxford Shoulder Scores favored debridement at 12 months (mean 34.3 versus 30.3; adjusted difference −4.2, 95% confidence interval −7.8 to −0.6, $P = 0.026$) in a trial that was stopped early for futility (Metcalfe, 2022).

Movement domains and what they mean clinically

Improvements in movement occurred with both approaches, but advantages differed by plane and did not change the overall comparative picture. Sandler observed relatively larger gains in abduction and external rotation with spacers, whereas forward flexion gains were larger with debridement. These directional differences did not translate into superior overall function for spacers (Sandler, 2024). Metcalfe reported no clinically meaningful advantage for spacers across secondary outcomes despite standardized rehabilitation and blinding, reinforcing that plane-specific gains do not overcome the absence of comparative benefit (Metcalfe, 2022).

Safety and durability

Device-specific risks and uncertain durability weigh against routine adoption. In Sandler, nearly one-half of spacer complications were migration or rupture, one-quarter of spacer reoperations were device revision or removal, and mean time to reverse shoulder arthroplasty was shorter after spacers than after debridement

(Sandler, 2024). Kunze's review emphasizes heterogeneity in thresholds and designs that can inflate apparent success in single-arm reports, underscoring the need for consistent definitions and comparative designs before concluding durable benefit (Kunze, 2023). Metcalfe's masked, intraoperative randomization and standardized rehabilitation minimize bias and provide the highest-quality signal to date that spacers do not confer comparative benefit (Metcalfe, 2022).

Meta-analyses

Comparative evidence does not show an advantage of the subacromial balloon spacer over alternative surgery (Daher, 2023; Sirignano, 2024). Daher's meta-analysis pooled three comparative studies (n = 311) and found no significant differences across pain, quality of life, function, or range of motion; for example, the pooled mean difference for visual analog scale pain was −0.11 (95% confidence interval −0.48 to 0.27), and range of motion contrasts were negligible for abduction (−2.6°) and forward elevation (−0.4°) (Daher, 2023). Sirignano's systematic review included twenty-seven studies spanning both comparative and noncomparative designs, with only six being comparative, which explains the difference between the total sample (n = 894) and the smaller pooled comparative analyses; its meta-analysis likewise reported a pooled visual analog scale effect of −0.11 (95% confidence interval −0.44 to 0.22) and no overall difference in active shoulder flexion (overall effect size 0.11, p=0.87) (Sirignano, 2024).

This pattern contrasts with noncomparative cohorts, which consistently showed within-group gains after balloon spacer implantation at 12 and 24 months in pain, function, and motion, even as pooled head-to-head comparisons remained null (Sirignano, 2024; Daher, 2023). Methodological quality was fair as measured by the Modified Coleman Methodology Score (mean 61.4 ± 11), and heterogeneity and small samples with clinically diverse patients limited precision (Sirignano, 2024; Daher, 2023). Outcomes may be better in carefully selected patients who can re-establish the glenohumeral force couple and who adhere to prescribed physical therapy; closer alignment between surgical and rehabilitation teams, with clearer reporting of postoperative rehabilitation, may further improve results (Sirignano, 2024).

Other evidence

Across studies, individuals improved meaningfully from baseline. In a level-one randomized controlled trial, use of a subacromial balloon spacer was compared with arthroscopic partial repair. The use of the spacer produced similar improvements to partial repair in the American Shoulder and Elbow Surgeons score and the Western Ontario Rotator Cuff Index without between-group pain differences, but the Constant–Murley score favored the balloon spacer at week six and month 24 (P = 0.021 and P = 0.05), and forward elevation favored the balloon spacer at every measured time point through 24 months ($P \leq 0.0048$ after week six) (n = 184) (Verma, 2022). In a retrospective series, the adjusted Constant–Murley score rose to 76.0 at approximately 33 months with gains in elevation, abduction, and external rotation (n = 39 shoulders) (Deranlot, 2017).

In a multicenter randomized controlled trial with debridement as the comparator, debridement alone outperformed debridement plus balloon on the Western Ontario Rotator Cuff Index and the Patient Global Impression of Change at 24 months, with the Oxford Shoulder Score trending the same way; range of motion data was not collected (n = 117) (Haque, 2025). In a separate report, adverse events and reoperations were infrequent and balanced in the randomized controlled trials, and no device-related serious events were reported (Verma, 2022). Operative time was shorter with the balloon spacer than partial repair, 44.6 minutes versus 71.2 minutes ($P < 0.0001$) (Verma, 2022). Operative time was shorter with InSpace than partial repair, 44.6 versus 71.2 minutes ($P < 0.0001$) (Verma, 2022). Deranlot reported one revision for spacer migration and limited

radiographic progression, with Hamada advancing one stage in four shoulders and three stages in one (Deranlot, 2017).

References

On 9/4/2025, 2025 we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were subacromial balloon spacer, biodegradable balloon spacer, shoulder spacer, rotator cuff tear, massive irreparable rotator cuff tear, reverse shoulder arthroplasty, tendon transfer, arthroscopic debridement. We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Agout C, Berhouet J, Spiry C, et al. Functional outcomes after non-operative treatment of irreparable massive rotator cuff tears: prospective multicenter study in 68 patients. *Orthop Traumatol Surg Res*. 2018;104(8 Suppl):S189–S192. Doi: 10.1016/j.otsr.2018.08.003.

American Academy of Orthopedic Surgeons. Management of rotator cuff injuries evidence-based clinical practice guideline. http://aaos.org/rccpg2025. Published August 18, 2025.

Berliner JL, Regalado-Magdos A, Ma CB, Feeley BT. Reverse Shoulder Arthroplasty. [Updated March 13, 2024]. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK574545/

Daher M, Pearl A, Zalaquett Z, et al. InSpace balloon for the management of massive irreparable rotator cuff tears: a systematic review and meta-analysis. *Clin Orthop Surg*. 2023;15(5):834-842. Doi:10.4055/cios23032.

Deranlot J, Herisson O, Nourissat G, et al. Arthroscopic subacromial spacer implantation in patients with massive irreparable rotator cuff tears: clinical and radiographic results of 39 retrospectives cases. *Arthroscopy*. 2017;33(9):1639-1644. Doi:10.1016/j.arthro.2017.03.029.

Haque A, Parsons H, Parsons N, et al. Two-year follow-up of a group-sequential, multicenter randomized controlled trial of a subacromial balloon spacer for irreparable rotator cuff tears of the shoulder (START:REACTS). *Am J Sports Med*. 2025;53(6):1291-1298. Doi:10.1177/03635465251326891.

Keener JD, Galatz LM, Teefey SA, et al. A prospective evaluation of survivorship of asymptomatic degenerative rotator cuff tears. *J Bone Joint Surg Am*. 2015;97(2):89–98. Doi: 10.2106/JBJS.N.00099.

Kunze KN, Moran J, Cecere R, et al. High rate of clinically meaningful achievement in outcomes after subacromial balloon spacer implantation for massive irreparable rotator cuff tears: a systematic review and meta-analysis. *Am J Sports Med*. 2024;52(1):286-294. Doi:10.1177/03635465231155916.

Metcalfe A, Parsons H, Parsons N, et al. Subacromial balloon spacer for irreparable rotator cuff tears of the shoulder (START:REACTS): a group-sequential, double-blind, multicenter randomized controlled trial. *Lancet*. 2022;399(10339):1954-1963. Doi:10.1016/S0140-6736(22)00652-3.

National Institute for Health and Care Excellence. Biodegradable subacromial spacer insertion for rotator cuff tears. Interventional procedures guidance [IPG775]. www.nice.org.uk/guidance/ipg775. Published November 15, 2023.

Sánchez-Losilla C, Ferré-Aniorte A, Ramírez-Haua J, Álvarez-Díaz P, Cugat R, Alentorn-Geli E. 'Irreparable' rotator cuff tears: tips and tricks to achieve arthroscopic repair. *Rev Asoc Argent Ortop Traumatol*. 2022;87(4):559–569. Doi: 10.15417/issn.1852-7434.2022.87.4.1604.

Sandler AB, Gil LG, Scanaliato JP, Green CK, Dunn JC, Parnes N. Subacromial balloon placement demonstrates no advantage over debridement in the treatment of massive irreparable rotator cuff tears: a dual-armed systematic review and meta-analysis of over 1000 patients. *Am J Sports Med*. 2024;52(4):1088-1097. Doi:10.1177/03635465231168127.

Sheean AJ, Rashid MS, Hartzler RU. Subacromial balloon spacer for the massive irreparable rotator cuff tear. *Curr Rev Musculoskelet Med*. 2024; Feb 17(2):47-57. Doi: 10.1007/s12178-023-09879-3.

Sirignano M, Nyland J, Krupp R. Subacromial balloon spacer massive rotator cuff tear treatment systematic review and meta-analysis: patient selection and physical therapy may be keys to outcome success. *Knee Surg Sports Traumatol Arthrosc*. 2024;32(9):2346-2357. Doi:10.1002/ksa.12331.

Tempelhof S, Rupp S, Seil R. Age-related prevalence of rotator cuff tears in asymptomatic shoulders. *J Shoulder Elbow Surg.* 1999;8(4):296-299. Doi:10.1016/s1058-2746(99)90148-9.

Varacallo MA, El Bitar Y, Sina RE, Mair SD. Rotator Cuff Syndrome. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing; 2024. Updated March 5, 2024. https://www.ncbi.nlm.nih.gov/books/NBK531506/

Verma N, Srikumaran U, Roden CM, et al. InSpace implant compared with partial repair for the treatment of full-thickness massive rotator cuff tears: a multicenter, single-blinded, randomized controlled trial. *J Bone Joint Surg Am*. 2022;104(14):1250-1262. Doi:10.2106/JBJS.21.00667.

Virk MS, Nicholson GP, Romeo AA, et al. Irreparable rotator cuff tears without arthritis treated with reverse total shoulder arthroplasty. *Open Orthop J*. 2016;10:296–308. Doi: 10.2174/1874325001610010296.

Yamamoto A, Takagishi K, Osawa T, et al. Prevalence and risk factors of a rotator cuff tear in the general population. *J Shoulder Elbow Surg*. 2010;19(1):116–120. Doi:10.1016/j.jse.2009.04.006.

US Food and Drug Administration. DEN200039 – FDA De Novo classification letter for resorbable shoulder spacer. Published 2021. https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200039.pdf.

Policy updates

9/4/2025: initial review date and clinical policy effective date: [ccp.04_effective_date]

Skin Substitutes for Chronic Wounds

Clinical Policy ID: CCP. 1552

Recent review date: 10/31/2025

Next review date: 2/28/2027

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

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis, by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

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).

References

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.

Bonham PA, Brunette G, Crestodina L, et al. 2021 guideline for management of patients with lower-extremity wounds due to diabetes mellitus and/or neuropathic disease: an executive summary. *J Wound Ostomy Continence Nurs*. 2022;49(3):267-285. Doi:10.1097/WON.0000000000000860.

Bus SA, Armstrong DG, Crews RT, et al. Guidelines on offloading foot ulcers in persons with diabetes (IWGDF 2023 update). *Diabetes Metab Res Rev*. 2024;40(3):e3647. Doi:10.1002/dmrr.3647.

Capo JT, Kokko KP, Rizzo M, et al. The use of skin substitutes in the treatment of the hand and upper extremity. *Hand (N Y)*. 2014;9(2):156-165. Doi:10.1007/s11552-013-9587-5.

Cardinal M, Eisenbud DE, Armstrong DG, et al. Serial measurements of wound area as a predictor of healing in chronic wounds. *Wound Repair Regen*. 2008;16(1):31-37. Doi:10.1111/j.1524-475X.2007.00331.x.

Chen P, Vilorio NC, Dhatariya K, et al. Guidelines on interventions to enhance healing of foot ulcers in people with diabetes (IWGDF 2023 update). *Diabetes Metab Res Rev*. 2024;40(3):e3644. Doi:10.1002/dmrr.3644.

Daneshi K, Arellano JA, Tepe S, Liu HY, Yenikomshian HA, Gillenwater J, Hultman CS, Ziembicki JA, Egro FM. Autologous skin cell suspension in burn care: a systematic review and meta-analysis of clinical outcomes. *J Burn Care Res*. Published online ahead of print September 19, 2025. Doi:10.1093/jbcr/iraf181.

Dardari D, Piaggesi A, Potier L, et al. Intact Fish Skin Graft to Treat Deep Diabetic Foot Ulcers. *NEJM Evidence*. 2024;3(12). Doi:10.1056/EVIDoa2400171.

Driver VR, Lavery LA, Reyzelman AM, et al. A clinical trial of Integra Template for diabetic foot ulcer treatment. Wound Repair Regen. 2015;23(6):891-900. Doi:10.1111/wrr.12357.

El Araby MM, Marcaccini G, Susini P, et al. From the ocean to the operating room: the role of fish skin grafts in burn management—a systematic review. *J Clin Med*. 2025;14(16):5750. Doi:10.3390/jcm14165750.

Eriksson E, Liu PY, Schultz GS, et al. Chronic wounds: treatment consensus. *Wound Repair Regen*. 2022;30(2):156–171. Doi:10.1111/wrr.12994.

Falanga V, Margolis D, Alvarez O, et al. Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. *Arch Dermatol*. 1998;134(3):293-300. Doi:10.1001/archderm.134.3.293.

Fitridge R, Chuter V, Mills J, et al. The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in people with diabetes mellitus and a foot ulcer. *Eur J Vasc Endovasc Surg*. 2023;66(4):454-483. Doi:10.1016/j.ejvs.2023.07.020.

Gibson ALF, Holmes JH 4th, Shupp JW, et al. A phase 3, open-label, controlled, randomized, multicenter trial evaluating the efficacy and safety of StrataGraft® construct in patients with deep partial-thickness thermal burns. *Burns*. 2021;47(5):1024-1037. Doi:10.1016/j.burns.2021.04.021.

Gould LJ, Alderden J, Aslam R, et al. Wound Healing Society Pressure Ulcer Guideline Working Group. WHS guidelines for the treatment of pressure ulcers—2023 update. *Wound Repair Regen*. 2024;32(1):6–33. Doi:10.1111/wrr.13130.

Halim AS, Khoo TL, Mohd Yussof SJ. Biologic and synthetic skin substitutes: an overview. *Indian J Plast Surg*. 2010;43(Suppl):S23-S28. Doi:10.4103/0970-0358.70712.

Haugh AM, Witt JG, Hauch A, et al. Amnion Membrane in Diabetic Foot Wounds: A Meta-analysis. *Plast Reconstr Surg Glob Open*. 2017;5(4):e1331. Doi:10.1097/GOX.0000000000001331.

Heimbach D, Luterman A, Rose J, et al. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn treatment. *J Burn Care Rehabil*. 2003;24(1):42-8. Doi:10.1097/00004630-200301000-00009.

Hickerson WL 4th, Remmers AE, Recker DP, et al. Twenty-five years' experience with cultured epidermal autografts. *J Burn Care Res*. 2019;40(2):157-165. Doi:10.1093/jbcr/iry061.

Hicks KE, Huynh MNQ, Jeschke M, Malic C. Dermal regenerative matrix use in burn patients: a systematic review. *J Plast Reconstr Aesthet Surg*. 2019;72(11):1741–1751. Doi:10.1016/j.bjps.2019.07.021

Hinchliffe RJ, Forsythe RO, Apelqvist J, et al. Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev*. 2020;36(S1):e3276. Doi:10.1002/dmrr.3276.

Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. *J Vasc Surg*. 2016;63(2 Suppl):3S-21S. Doi:10.1016/j.jvs.2015.10.003.

Holmes Iv JH, Molnar JA, Carter JE, et al. A Comparative Study of the ReCell® Device and Autologous Spit-Thickness Meshed Skin Graft in the Treatment of Acute Burn Injuries. J Burn Care Res. 2018;39(5):694-702. Doi:10.1093/jbcr/iry029.

Hundeshagen G, Collins VN, Wurzer P, et al. A Prospective, Randomized, Controlled Trial Comparing the Outpatient Treatment of Pediatric and Adult Partial-Thickness Burns with Suprathel or Mepilex Ag. J Burn Care Res. 2018;39(2):261-267. Doi:10.1097/BCR.0000000000000584.

Jones JE, Nelson EA, Al-Hity A. Skin grafting for venous leg ulcers. *Cochrane Database Syst Rev*. 2013;(1):CD009402. Doi:10.1002/14651858.CD009402.pub3.

Kavros SJ, Dutra T, Gonzalez-Cruz R, et al. The use of PriMatrix, a fetal bovine acellular dermal matrix, in healing chronic diabetic foot ulcers: a prospective multicenter study. *Adv Skin Wound Care*. 2014;27(8):356-62. Doi:10.1097/01.ASW.0000451891.87020.69.

Kumar RJ, Kimble RM, Boots R, Pegg SP. Treatment of partial-thickness burns: a prospective, randomized trial using Transcyte. ANZ J Surg. 2004;74(8):622-626. Doi:10.1111/j.1445-1433.2004.03106.x.

Lavery LA, Fulmer J, Shebetka KA, et al. The efficacy and safety of Grafix(®) for the treatment of chronic diabetic foot ulcers: results of a multi-centre, controlled, randomised, blinded, clinical trial. Int Wound J. 2014;11(5):554-560. Doi:10.1111/iwj.12329.

Lavery LA, Suludere MA, Attinger CE, et al. WHS (Wound Healing Society) guidelines update: Diabetic Foot Ulcer Treatment Guidelines. *Wound Repair Regen*. 2024;32(1):34–46. Doi:10.1111/wrr.13133.

Lu W, Hu M, Zhang Z, Slaughter J, Hingorani A, Oropallo A. Meta-analysis of cellular and acellular tissue-based products demonstrates improvement of diabetic foot ulcer healing despite age and wound size. *JVS–Vasc Insights*. 2025;3:100215. Doi:10.1016/j.jvsvi.2025.100215.

Marston W, Tang J, Kirsner RS, Ennis W. Wound Healing Society 2015 update on guidelines for venous ulcers. *Wound Repair Regen*. 2016;24(1):136–144. Doi:10.1111/wrr.12394.

Marston WA, Hanft J, Norwood P, Pollak R; Dermagraft Diabetic Foot Ulcer Study Group. The efficacy and safety of Dermagraft in improving the healing of chronic diabetic foot ulcers: results of a prospective randomized trial. *Diabetes C¹are*. 2003;26(6):1701-1705. Doi:10.2337/diacare.26.6.1701.

Mostow EN, Haraway GD, Dalsing M, Hodde JP, King D. Effectiveness of an extracellular matrix graft (OASIS Wound Matrix) in the treatment of chronic leg ulcers: a randomized clinical trial. *J Vasc Surg*. 2005;41(5):837-843. Doi:10.1016/j.jvs.2005.02.042.

Nair HKR, Mrozikiewicz-Rakowska B, Pinto DS, et al. Use of wound antiseptics in practice. Wounds International. Published October 3, 2023. https://woundsinternational.com/consensus-documents/use-of-wound-antiseptics-in-practice/.

O'Donnell TF Jr, Passman MA, Marston WA, et al. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg*. 2014;60(2 Suppl):3S-59S. Doi:10.1016/j.jvs.2014.04.049.

Putri IL, Sindhu FC, Aisyah IF, Pramanasari R, Wungu CDK. Comparison of combination skin substitutes and skin grafts versus skin grafts only for treating wounds measured by Vancouver Scar Scale: a comprehensive meta-analysis. *SAGE Open Med*. 2024;12:1–13. Doi:10.1177/20503121241266342.

Ruiz-Muñoz M, Martinez-Barrios FJ, Cervera-Garvi P, et al. Fish skin grafts versus standard of care on wound healing of chronic diabetic foot ulcers: A systematic review and meta-analysis. *Prim Care Diabetes*. 2024;18(3):291-298. Doi:10.1016/j.pcd.2024.03.008.

Santema TB, Poyck PPC, Ubbink DT. Skin grafting and tissue replacement for treating foot ulcers in people with diabetes. *Cochrane Database Syst Rev*. 2016;2:CD011255. Doi:10.1002/14651858.CD011255.pub2.

Schaper NC, van Netten JJ, Apelqvist J, et al. Practical guidelines on the prevention and management of diabetes-related foot disease (IWGDF 2023 update). *Diabetes Metab Res Rev*. 2024;40(3):e3657. Doi:10.1002/dmrr.3657.

Serena TE, Bayliff SW, Brosnan PJ. Bacterial protease activity: a prognostic biomarker of early wound infection. *J Wound Care*. 2022;31(4):352-355. Doi:10.12968/jowc.2022.31.4.352.

Serena TE, Lullove E, Kirsner RS, et al. Aseptically processed dehydrated human amnion and chorion allograft improves healing of chronic venous leg ulcers: a prospective, randomized, controlled, multicenter trial. *Plast Reconstr Surg*. 2022;150(4):917-926. Doi:10.1097/PRS.0000000000009581.

Serena TE, Ya-wen R, Zelen CM, et al. A multicenter, randomized, controlled clinical trial evaluating the use of dehydrated human amnion/chorion membrane allografts and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. *Wound Repair Regen*. 2014;22(6):688-93. Doi:10.1111/wrr.12227.

Sheehan P, Jones P, Caselli A, et al. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. *Diabetes Care*. 2003;26(6):1879-1882. Doi:10.2337/diacare.26.6.1879.

Snyder D, Sullivan N, Margolis D, Schoelles K. Skin substitutes for treating chronic wounds. Agency for Healthcare Research and Quality (US); 2020. Published February 2, 2020. Available at: https://www.ncbi.nlm.nih.gov/books/NBK554220/.

Sui L, Xie Q, Jiang H, et al. Effectiveness and safety of dermal matrix used for diabetic foot ulcer: a systematic review and meta-analysis of randomized controlled trials. *BMC Endocr Disord*. 2024;24:23. Doi:10.1186/s12902-024-01550-3.

U.S. Food and Drug Administration. Premarket approval (PMA): Apligraf (Graftskin), PMA number: P950032. Decision date: May 22, 1998. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P950032.

U.S. Food and Drug Administration. Biobrane brand temporary wound-dressing: 510(k) premarket notification K801635. Decision date: August 4, 1980. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K801635.

U.S. Food and Drug Administration. Biobrane temporary wound dressing and Biobrane glove: 510(k) premarket notification K242146. Decision date: December 17, 2024. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K242146.

U.S. Food and Drug Administration. Consolidation of wound-care products containing live cells. Accessed November 2, 2025. Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/consolidation-wound-care-products-containing-live-cells.

U.S. Food and Drug Administration. Premarket Approval (PMA) P000036: Dermagraft. Decision date: September 28, 2001. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P000036.

U.S. Food and Drug Administration. Epicel (cultured epidermal autografts) humanitarian device exemption decision summary H990002. Decision date: October 25, 2007. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm?id=H990002.

U.S. Food and Drug Administration. Premarket approval (PMA) supplement S008, Integra LifeSciences Corp., Integra dermal regeneration template. Decision date: April 19, 2002. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P900033S008.

U.S. Food and Drug Administration. Premarket approval (PMA) P900033S042: Integra dermal regeneration template, Omnigraft dermal regeneration matrix. Decision date: January 7, 2016. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P900033S042.

U.S. Food and Drug Administration. Marigen wound dressing: 510(k) premarket notification K132343. Decision date: October 23, 2013. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K132343.

U.S. Food and Drug Administration. Marigen wound extra: 510(k) premarket notification K190528. Decision date: July 10, 2019. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?id=K190528.

U.S. Food and Drug Administration. Oasis wound matrix: 510(k) premarket notification K061711. Decision date: July 19, 2006. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K061711.

U.S. Food and Drug Administration. Package Insert – Stratagraft. Published 2021. Available at: https://www.fda.gov/media/150129/download.

U.S. Food and Drug Administration. 510(k) summary: PriMatrix Dermal Repair Scaffold (K083440). Decision date December 12, 2008. Accessed November 2, 2025. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf8/K083440.pdf.

U.S. Food and Drug Administration. Premarket Approval BP170122: ReCell autologous cell harvesting device. Decision approved September 20, 2018. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=BP170122.

U.S. Food and Drug Administration. 510(k) premarket notification: Suprathel wound and burn dressing K090160. Decision date: May 20, 2009. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K090160.

U.S. Food and Drug Administration. Premarket approval for TransCyte human fibroblast-derived temporary skin substitute P960007. Published March 18, 1997. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P960007.

van den Bosch AS, Verwilligen RAF, Pijpe A, et al. Outcomes of dermal substitutes in burns and burn scar reconstruction: a systematic review and meta-analysis. *Wound Repair Regen*. 2024;32(6):960–978. Doi:10.1111/wrr.13226.

van den Bosch AS, Verwilligen RAF, Pijpe A, et al. Indications for the use of dermal substitutes in patients with acute burns and in reconstructive surgery after burns: A systematic review. *Wound Repair Regen*. 2025;33(1):e13248. doi:10.1111/wrr.13248.

Vecin NM, Kirsner RS. Skin substitutes as treatment for chronic wounds: current and future directions. *Front Med (Lausanne)*. 2023; 10:1154567. Doi:10.3389/fmed.2023.1154567.

Veves A, Falanga V, Armstrong DG, Sabolinski ML; Apligraf Diabetic Foot Ulcer Study. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: a prospective randomized multicenter clinical trial. *Diabetes Care*. 2001;24(2):290-295. Doi:10.2337/diacare.24.2.290.

Walters J, Cazzell S, Pham H, Vayser D, Reyzelman A. Healing Rates in a Multicenter Assessment of a Sterile, Room Temperature, Acellular Dermal Matrix Versus Conventional Care Wound Management and an Active Comparator in the Treatment of Full-Thickness Diabetic Foot Ulcers. *Wounds*. 2016;28(1):1-10. PMID: 26933467.

Wasiak J, Cleland H, Campbell F, Spinks A. Dressings for superficial and partial thickness burns. *Cochrane Database Syst Rev*. 2013;(3):CD002106. Doi:10.1002/1465188.CD002106.pub4.

Zelen CM, Serena TE, Denoziere G, Fetterolf DE. A prospective randomised comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. *Int Wound J*. 2013;10(5):502-507. Doi:10.1111/iwj.12097.

Policy updates

9/30/2025 initial review date and clinical policy effective date: [ccp.04_effective_date]

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 extend through the dermis, without tendon, muscle, capsule, or	Santema, 2016	Hingorani, 2016	Veves, 2001	A

			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 bone exposed, when used in conjunction with standard diabetic ulcer care."	Sui, 2024	Hingorani, 2016	Driver, 2015	B
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." (device-cleared for wound management, not etiology-specific approval)	None found as of Nov 2025	—	Kavros, 2014 (Prospective cohort)	C
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, and Cellular and Tissue-based Products / Tier 3	—	Not Food and Drug Administration -approved for wound indications.	None found as of Nov 2025	—	Lavery, 2014. Evidence from small randomized controlled trial; industry sponsorship noted.	B

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	—	Not Food and Drug Administration-approved for wound indications.	Haugh, 2017	—	Serena, 2014. Evidence base consists of small randomized controlled trials	B

	Products / Tier 3					with sponsorship.	
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 Regeneratio n Template	Premarket Approval / Tier 1	P900033 (Jan 7, 2016)	“Postexcisiona l 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-thickne ss thermal burns prior to autograft; and mid-dermal to indeterminate depth burns expected to	None found as of Nov 2025	None found as of Nov 2025	Kumar, 2004	B

			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 least 15 years."	Daneshi, 2025 (conference abstract only)	None found as of Nov 2025	Holmes, 2018	B
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-	Wasiak, 2013	None found as of Nov 2025	Kumar, 2004: pediatric partial-thickness burns; faster re-epithelialization vs silver sulfadiazine;	B

			cleared for wound management, not etiology-specific approval)			comparator TransCyte arm reported.	
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)

Transcatheter Therapy for Severe Tricuspid Insufficiency

Clinical Policy ID: CCP.1551

Recent review date: 10/31/2025

Next review date: 2/28/2027

Policy contains: Evoque; heart failure; TriClip; tricuspid insufficiency; tricuspid valve repair; tricuspid valve replacement.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis, by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

Transcatheter edge-to-edge repair and transcatheter tricuspid valve replacement procedures for severe tricuspid insufficiency (also called tricuspid regurgitation) are investigational/not clinically proven and, therefore, not medically necessary.

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Guideline-directed medical therapy

- Surgical tricuspid valve repair
- Surgical tricuspid valve replacement

Background

Tricuspid insufficiency (or regurgitation) results from structural abnormalities of the tricuspid valve complex that cause incomplete valve closure and retrograde flow of blood from the right ventricle into the right atrium during systole. In U.S. adults, the incidence of tricuspid regurgitation ranges from 5% to 20%. Tricuspid regurgitation-related morbidity and mortality increase with severity (Mulla, 2024).

Tricuspid regurgitation is categorized as either primary, caused by intrinsic abnormalities in the tricuspid valve apparatus, or secondary, caused by right atrial or ventricular dilatation. A third category, tricuspid regurgitation related to a cardiac procedure such as endomyocardial biopsy or implantable electronic device, can develop if the device interferes with the tricuspid valve leaflets or subvalvular apparatus, or if right ventricular pacing leads to right ventricular remodeling (O'Gara, 2025).

A combination of structural, qualitative, semiquantitative, and quantitative measures using echocardiography is used to assess valvular morphology, severity of tricuspid regurgitation, and adjunctive cardiac features. Cardiac magnetic resonance and computed tomography may further define complex tissue structures. The severity of tricuspid regurgitation is commonly graded as mild (1+), moderate (2+), or severe (3+). More recently, severe disease may be further graded as massive or torrential. Guideline-directed diagnosis of severe tricuspid regurgitation is based on assessment of regurgitant jet area with vena contracta and presence of hepatic vein reverse flow. Severe (3+) classification is defined by a vena contracta diameter of at least 7 millimeters, effective regurgitant orifice area of at least 40 square millimeters, and/or a regurgitant volume of at least 45 millilters per beat (Ambrosino, 2024).

Patients with severe tricuspid regurgitation usually present with signs or symptoms of right-sided heart failure. The prognostic impact of a tricuspid regurgitation diagnosis is well recognized, but the effect of its correction is less so. Treatment options are limited to guideline-directed medical therapy for symptom relief and surgery. Surgical intervention for isolated tricuspid regurgitation is relatively uncommon in the United States due to a perceived high in-hospital mortality rate of up to 10%, despite stringent selection criteria. Instead, surgery is performed typically for those who have another primary indication for surgery, such as concomitant mitral or aortic valvular disease, or to prevent later development of severe tricuspid regurgitation in patients with progressive tricuspid disease. Earlier referral and more effective techniques may improve patient outcomes (Ambrosino, 2024).

Transcatheter tricuspid valve interventions

Minimally invasive, transcatheter tricuspid valve interventions have emerged as potential options for tricuspid valve repair and replacement. The options for transcatheter repair are leaflet coaptation devices (tricuspid valve edge-to-edge repair) and annuloplasty. Transcatheter replacement options include orthotopic replacement of the tricuspid valve and heterotopic caval valve implantation (Ambrosino, 2024).

As of this writing, two transcatheter options have received regulatory approval for clinical use in the United States. The TriClip G4 transcatheter tricuspid valve repair system (Abbott Medical, St. Paul, Minnesota) is delivered via a transfemoral venous approach under transesophageal echocardiographic guidance. It uses a specialized clip to grasp and join together the edges of the leaking valve leaflets, which creates a stable double orifice. This device is indicated for improving quality of life and functional status in patients with symptomatic severe tricuspid regurgitation despite optimal medical therapy, who are at intermediate or greater risk for surgery and in whom transcatheter edge-to-edge valve repair is clinically appropriate and is expected to reduce tricuspid regurgitation

severity to moderate or less, as determined by a multidisciplinary heart team. Regulatory approval is based on the results of the TRILUMINATE Pivotal Trial (Kar, 2025; ClinicalTrials.gov identifier NCT03904147; U.S. Food and Drug Administration, 2024b).

The Edwards Evoque Tricuspid Valve Replacement System (Edwards Lifesciences LLC, Irvine, California) is made from bovine pericardial tissue, uses a transfemoral venous approach, and comes in three sizes. It replaces the native tricuspid heart valve without concomitant removal of the failed native valve. This device is indicated for the improvement of health status in patients with symptomatic severe tricuspid regurgitation despite optimal medical therapy, in whom tricuspid valve replacement is deemed appropriate by a heart team. Regulatory approval was based on the safety and effectiveness results from the TRISCEND II pivotal trial (ClinicalTrials.gov identifier NCT04482062, U.S. Food and Drug Administration, 2024a).

Findings

Isolated severe tricuspid regurgitation is associated with high surgical risk and long-term mortality risk, and advances in medical and surgical management have not lowered mortality rates (Suc, 2025). Transcatheter options are recent additions that are safe and improve the severity of tricuspid regurgitation and health status in patients at high or prohibitive surgical risk, but evidence is lacking on mortality and heart failure hospitalization rates, efficacy in patients with mild or moderate tricuspid regurgitation, and long-term outcomes (Donal, 2025; Hahn, 2025; Sorajja, 2023). Current guidelines acknowledge the limited available evidence and provide mixed recommendations for clinical use outside of research protocols.

Guidelines

The current American College of Cardiology guideline on valvular heart disease acknowledges a growing interest in catheter-based therapies for tricuspid regurgitation but issued no recommendation (Otto, 2020).

In 2025, an American College of Cardiology writing committee summarized the most important developments for patients with severe tricuspid regurgitation, with emphasis on those with secondary tricuspid regurgitation in the chronic setting. Transcatheter interventions are in the early stages of new device development and testing in clinical trials. Most current trial data reflect a patient population with high or prohibitive surgical risk. Ongoing studies are comparing the effectiveness of transcatheter options to optimal medical therapy; comparisons to isolated tricuspid valve surgery or to other transcatheter options have not been conducted. The writing committee recommends counseling patients on expected benefits and risks with both surgical and available transcatheter interventions within a multidisciplinary team consensus and shared decision-making (O'Gara, 2025).

The European Society of Cardiology and the European Association for Cardio-Thoracic Surgery joint guideline on the management of valvular heart disease addressed all transcatheter tricuspid valve options available in the European Union, including TriClip and Evoque. The guideline states transcatheter tricuspid valve treatment should be considered to improve quality of life and right ventricular remodeling in high-risk patients with symptomatic severe tricuspid regurgitation despite optimal medical therapy, and in the absence of severe right ventricular dysfunction or pre-capillary pulmonary hypertension (Class IIa recommendation; Level of evidence A based on data derived from randomized controlled trials or meta-analyses) (Praz, 2025).

The National Institute for Health and Care Excellence (2022) states transcatheter tricuspid valve leaflet repair should only be used with special arrangements for clinical governance, consent, and audit or research. For individuals with severe and symptomatic tricuspid regurgitation, evidence on efficacy is limited in quantity and quality, and there are serious but well-recognized complications. For individuals with mild or moderate tricuspid regurgitation, evidence on the safety and efficacy is of inadequate quantity and quality.

Evidence review

Data from three randomized controlled trials demonstrate the safety and efficacy of transcatheter tricuspid valve repair (TriClip) and replacement (Evoque) procedures in reducing the severity of tricuspid regurgitation in more than 80% of cases where anatomical suitability was confirmed. These results and improvement in health status were sustained up to one year for Evoque and up to two years for TriClip. The effects of transcatheter interventions on rates of heart failure hospitalization and mortality may be realized with longer follow up, as evidence for TriClip suggests.

Transcatheter edge-to-edge repair is the most extensively studied transcatheter technique for severe tricuspid regurgitation. Compared to TriClip, Evoque is associated with more procedural complications but a lower rate of residual tricuspid regurgitation. It appears to be most suitable for patients who have anatomy that precludes repair, and it has the ability to treat a wider range of tricuspid regurgitation pathologies.

Transcatheter tricuspid valve edge-to-edge repair (TriClip)

The evidence for the TriClip procedure consists of results from the TRILUMINATE Pivotal trial carried out in the United States (n = 350; Jorde, 2024; Kar, 2025; Naik, 2025; Sorajja, 2023) and from the TRI.Fr randomized controlled trial in Europe (n = 300; Donal, 2025). Both trials compared the safety and efficacy of optimized medical therapy with and without TriClip for treating severe, symptomatic, isolated tricuspid regurgitation. Both trials reported outcomes at 12 months. TRILUMINATE also reported full two-year follow-up data (Kar, 2025) and three-year follow-up data from a cohort of TriClip recipients (Nickenig, 2024).

The main eligibility criteria for inclusion in both of these trials were New York Heart Association class II to IV heart failure; on guideline-directed medical therapy and stable for at least 30 days; free from other cardiovascular conditions requiring intervention; and considered intermediate-to-high risk for surgery. In general, participants with highly advanced disease (e.g., severe kidney failure, liver failure, advanced cardiorenal syndrome, or pulmonary artery systolic pressure > 60 millimeters of mercury) were excluded. The mean age of participants was 78 years, and a slight majority were women. Participants had significantly impaired quality of life at baseline, and a high proportion experienced heart failure hospitalizations in the previous year (Donal, 2025; Sorajja, 2023).

TriClip safety

Transcatheter tricuspid valve edge-to-edge repair using TriClip is a safe procedure in experienced hands. TriClip was successfully implanted in at least 97% of participants. TriClip was associated with low rates of periprocedural adverse events, which were comparable to the control arms. At 12 months, rates of major cardiovascular events, deaths, and hospitalizations were similar between study arms. Single-leaflet device attachments occurred in 5.2% in the TRI.Fr trial and 7.0% in the TRILUMINATE trial (Donal, 2025; Sorajja, 2023).

In the TRI.Fr trial, three recipients of TriClip required tricuspid valve surgery, five required a cardiac electronic rhythm device, and nine experienced a major bleed. These results did not differ significantly from the control group (Donal, 2025). In the TRILUMINATE trial, five TriClip recipients and five in the control group required a cardiac electronic rhythm device (Sorajja, 2023).

TriClip efficacy

The TRILUMINATE and TRI.Fr trials used composite clinical endpoints at 12 months as their primary outcome measures. The composite endpoints differed in composition but included elements of objective adverse cardiovascular event data and patient-reported outcome measures (Donal, 2025; Sorajja, 2023).

At year one, the results of the primary endpoint favored the TriClip arm, driven by the magnitude of improvement in patient-reported outcome measures, including quality of life, rather than by changes in the rates of cardiovascular hospitalization or cardiovascular death. Significantly more TriClip recipients experienced a reduction in the severity of tricuspid regurgitation, from severe or greater to moderate or less, than those on optimized medical therapy alone. These results suggest a correlation between quality-of-life improvement and

reduction in tricuspid regurgitation up to one year following the procedure. The trials reached different conclusions regarding the impact of TriClip on the six-minute walk test distance (Donal, 2025; Sorajja, 2023).

A separate analysis of 98 participants with transvalvular cardiac implantable electronic devices at baseline found TriClip repair was safe and effective and did not affect device function up to one year (Naik, 2025). Jorde (2024) observed potential benefits for TriClip repair in improving end organ renal and liver function, but additional research is needed to assess whether the statistically significant improvements are clinically meaningful and reduce mortality or heart failure hospitalization.

At year two, results of the TRILUMINATE trial showed sustained benefits of TriClip repair versus controls in terms of improved tricuspid regurgitation, health status, and comparable adverse event rates. Notably, 59% of the control participants crossed over to the TriClip group before the two-year follow-up. From year one to year two, the TriClip group showed a significantly greater reduction in the rate of heart failure hospitalization and freedom from all-cause mortality, tricuspid valve surgery, and tricuspid valve intervention compared with medical therapy. These findings were driven by the crossover of controls to the TriClip group, who were more symptomatic and had more severe tricuspid regurgitation, higher hospitalization rates, and worsened functional score than those who remained in the control group. Rates of all-cause mortality and tricuspid valve surgery remained similar between groups (Kar, 2025).

At year three, in a subset of 98 TRILUMINATE TriClip recipients, major adverse events included cardiovascular mortality (n = 18), myocardial infarction (n = 1), stroke (n = 4), and new onset of renal failure (n = 8). Benefits in reduced tricuspid regurgitation, favorable remodeling of the right heart, and improved heart failure symptoms were maintained. There was a 75% reduction in heart failure hospitalizations, from 0.56 events/patient-year in year one to 0.14 events/patient-year in year three ($P < .0001$). Those who achieved a reduction in tricuspid regurgitation from severe or greater to moderate or less at 30 days were less likely to experience heart failure hospitalization or death by year three compared with those who maintained severe or greater tricuspid regurgitation at 30 days (30.7% vs. 50.7%, hazard ratio = 0.48, 95% confidence interval 0.25 to 0.93, $P = .026$). Quality of life, measured by the Kansas City Cardiomyopathy Questionnaire score, initially improved in year one, but declined at year three, yet still maintained a 10-point improvement over baseline (Nickenig, 2024).

Transcatheter tricuspid valve replacement (Evoque*)*

The evidence for transcatheter tricuspid valve replacement using Evoque consists of results from the TRISCEND II pivotal randomized controlled trial (Arnold, 2025; Hahn, 2025). Eligibility criteria included participants at least 18 years of age with severe, massive, or torrential tricuspid regurgitation, who were eligible for valve replacement, and had either signs or symptoms of tricuspid regurgitation or a recent hospitalization for associated heart failure despite medical therapy. The vast majority of enrollees were white women with a mean age of 79 years. There was a high prevalence of hypertension, atrial fibrillation, left ventricular ejection fraction of more than 50%, and substantially impaired health status at baseline. Participants also had a high prevalence of renal insufficiency and history of bleeding (Hahn, 2025).

Participants were randomized to the valve-replacement group (n = 267) or medical therapy alone (n = 133). The hierarchical composite primary outcome was death from any cause, implantation of a right ventricular assist device or heart transplantation, subsequent tricuspid-valve intervention, heart failure hospitalization, an improvement of at least 10 points in the score on the Kansas City Cardiomyopathy Questionnaire overall summary, an improvement of at least one New York Heart Association functional class, and an improvement of at least 30 meters on the six-minute walk test distance. Investigators used the win ratio to analyze the composite endpoint, which prioritizes each element based on clinical importance in terms of the proportion of successful outcomes compared to unsuccessful ones (Hahn, 2025).

Evoque safety

Most adverse clinical events occurred peri-procedurally, driven primarily by severe bleeding (10.4% in the valve replacement group vs. 1.5% in controls, P = .003) and conduction disorders leading to new pacemaker implantation (15.8% vs. 0%, P < .001).

Evoque efficacy

At 30 days, the rates of death from any cause (P = .87) and death from cardiovascular causes (P = .85) were similar between groups. At year one, the primary composite endpoint favored valve replacement over medical therapy (win ratio 2.02, 95% confidence interval 1.56 to 2.62, P < .001), driven primarily by improvements in symptoms and quality of life. Echocardiographic outcomes favored the valve-replacement group, in whom tricuspid regurgitation was decreased to a mild degree or less in 95.2% compared with 2.3% of those in the control group. Authors observed improvements in right ventricular reverse remodeling and in markers of liver congestion (Hahn, 2025).

Adding transcatheter valve replacement resulted in substantial improvement in participants' symptoms, function, and quality of life over medical therapy alone. The magnitude of the health status benefit was directly related to the baseline severity of tricuspid regurgitation. Moderate benefits were evident 30 days after the procedure, continued to improve through the first six months, and were maintained through year one (Arnold, 2025).

References

On 9/23/2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "tricuspid valve insufficiency" (MeSH), "tricuspid valve insufficiency," "tricuspid valve regurgitation," "TriClip," and "EVOQUE." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Ambrosino M, Sangoi M, Monzer N, et al. Tricuspid regurgitation: A review of current interventional management. *J Am Heart Assoc*. 2024;13(6):e032999. Doi: 10.1161/JAHA.123.032999.

Arnold SV, Hahn RT, Thourani VH, et al. Quality of life after transcatheter tricuspid valve replacement: 1-year results from TRISCEND II pivotal trial. *J Am Coll Cardiol*. 2025;85(3):206-216. Doi: 10.1016/j.jacc.2024.10.067.

ClinicalTrials.gov identifier NCT03904147. TRILUMINATE Pivotal Trial. Last update posted December 19, 2024. https://clinicaltrials.gov/study/NCT03904147.

ClinicalTrials.gov identifier NCT04482062. TRISCEND II Pivotal Trial.https://www.clinicaltrials.gov/study/NCT04482062?term=TRISCEND%20II%20trial&rank=1. Last update posted August 15, 2025.

Donal E, Dreyfus J, Leurent G, et al. Transcatheter edge-to-edge repair for severe isolated tricuspid regurgitation: The TRI.Fr randomized clinical trial. *JAMA*. 2025;333(2):124-132. Doi: 10.1001/jama.2024.21189.

Hahn RT, Makkar R, Thourani VH, et al. Transcatheter valve replacement in severe tricuspid regurgitation. *N Engl J Med*. 2025;392(2):115-126. Doi: 10.1056/NEJMoa2401918.

Jorde UP, Benza R, McCarthy PM, et al. Impact of renal and liver function on clinical outcomes following tricuspid valve transcatheter edge-to-edge repair. *J Am Coll Cardiol*. 2024;84(25):2446-2456. Doi: 10.1016/j.jacc.2024.08.044.

Kar S, Makkar RR, Whisenant BK, et al. Two-year outcomes of transcatheter edge-to-edge repair for severe tricuspid regurgitation: The TRILUMINATE pivotal randomized controlled trial. *Circulation*. 2025;151(23):1630-1638. Doi: 10.1161/circulationaha.125.074536.

Mulla S, Asuka E, Bora V, et al. Tricuspid Regurgitation. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; Updated October 6, 2024. https://www.ncbi.nlm.nih.gov/books/NBK526121/.

Naik H, Price MJ, Kapadia S, et al. Tricuspid transcatheter edge-to-edge repair in patients with transvalvular CIED leads: The TRILUMINATE pivotal trial. *JACC Clin Electrophysiol*. 2025;11(5):1012-1020. Doi: 10.1016/j.jacep.2025.01.001.

National Institute for Health and Care Excellence. Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation. Interventional procedures guidance. Reference number: IPG731. https://www.nice.org.uk/guidance/ipg731. Published July, 27, 2022.

Nickenig G, Lurz P, Sorajja P, et al. Percutaneous edge-to-edge repair for tricuspid regurgitation: 3-year outcomes from the TRILUMINATE study. *JACC Cardiovasc Interv*. 2024;17(18):2113-2122. Doi: 10.1016/j.jcin.2024.05.036.

O'Gara PT, Lindenfeld J, Hahn RT, et al. 10 issues for the clinician in tricuspid regurgitation evaluation and management: 2025 ACC expert consensus decision pathway: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2025. Doi: 10.1016/j.jacc.2025.07.002.

Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *J Thorac Cardiovasc Surg*. 2021;162(2):e183-e353. Doi: 10.1016/j.jtcvs.2021.04.002.

Praz F, Borger MA, Lanz J, et al. 2025 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2025, ehaf194. Doi: 10.1093/eurheartj/ehaf194.

Sorajja P, Whisenant B, Hamid N, et al. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023;388(20):1833-1842. Doi: 10.1056/NEJMoa2300525.

Suc G, Mesnier J, Cailliau A, et al. Survival outcomes in isolated severe tricuspid regurgitation according to therapeutic modalities: A systematic review and meta-analysis. *Open Heart*. 2025;12(1):e002986. Doi: 10.1136/openhrt-2024-002986.

U.S. Food and Drug Administration. Edwards EVOQUE tricuspid valve replacement system. Summary of safety and effectiveness data (SSED). https://www.accessdata.fda.gov/cdrh_docs/pdf23/P230013B.pdf. Approved February 1, 2024.(a)

U.S. Food and Drug Administration. TriClip G4 system. Summary of safety and effectiveness data (SSED). https://www.accessdata.fda.gov/cdrh_docs/pdf23/P230007B.pdf. Approved April 1, 2024.(b)

Policy updates

11/3/2025 initial review date and clinical policy effective date: TBD

Transperineal laser ablation of the prostate for benign prostatic hyperplasia

Clinical Policy ID: CCP.1548

Recent review date: 9/30/2025

Next review date: 1/31/2027

Policy contains: Benign prostatic hyperplasia; EchoLaser X4; SoracteLite; Transperineal laser ablation.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis, by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

Transperineal laser ablation of the prostate is investigational/not clinically proven and, therefore, not medically necessary for the treatment of benign prostatic hyperplasia.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Guideline-directed therapy (Lerner, 2023):

- Medical therapy, alone or in combination (alpha blockers, 5-alpha reductase inhibitors, phosphodiesterase-5 inhibitors).
- Transurethral resection of the prostate.
- Simple prostatectomy.

- Transurethral incision of the prostate
- Transurethral vaporization of the prostate.
- Photoselective vaporization of the prostate.
- Prostatic urethral lift.
- Water vapor thermal therapy.
- Laser enucleation.
- Robotic waterjet treatment.
- Prostate artery embolization.
- Temporary implanted prostatic devices.

Background

Benign prostatic hyperplasia, also known as benign prostatic hypertrophy, is a nonmalignant growth of prostate tissue and is relatively common in older individuals with a prostate. The condition is marked by symptoms of the lower urinary tract, urinary retention, or infections due to incomplete bladder emptying. Some cases will not require treatment but can be addressed by watchful waiting to ensure worsening of symptoms is limited. Other cases can be treated conservatively with alpha blockers, 5-alpha reductase inhibitors, phosphodiesterase-5 inhibitors, antimuscarinics, or a combination. However, these medications are not always effective and are associated with elevated risk of ejaculatory and erectile dysfunction (Ng, 2025).

For cases requiring surgery, transurethral approaches and enucleation procedures have largely replaced open prostatectomy as preferred surgical options. Minimally invasive surgical options such as transurethral microwave thermotherapy, water vapor or steam infusion therapy, and prostatic urethral internal lateral suturing have emerged, offering shorter time in the operating room, faster recovery, and fewer side effects (Ng, 2025).

Transperineal laser ablation of the prostate is an emerging treatment for benign prostatic hyperplasia associated with moderate-to-severe lower urinary tract symptoms. It is a minimally invasive, ultrasound-guided procedure that applies focused heat from a laser light into the prostate to ablate the enlarged tissue *in situ*. The laser forms an ellipsoidal area of coagulative necrosis, which the body resorbs. The procedure can be performed in an outpatient setting under local anesthesia (Sessa, 2022).

The U.S. Food and Drug Administration has issued 510(k) premarket clearance to the EchoLaser X4 (Elesta SpA, Calenzano, Italy). It is intended for necrotizing or coagulating soft tissue through interstitial irradiation for use in medicine and surgery, including urology, at a wavelength of 1064 nanometers (U.S. Food and Drug Administration, 2018, 2022). The manufacturer describes the EchoLaser as a “micro-invasive, multi-fiber” approach in which up to four flexible quartz optical fibers with a small diameter (300 micron) and a flat tip transmit laser light through fine 21-gauge needles inserted percutaneously. The procedure can be carried out with transrectal ultrasound guidance for real-time positioning and treatment monitoring. The device is also called SoracteLite™ when used specifically for urological indications, to differentiate from Echolaser thermal ablation used for other indications (Elesta-echolaser SpA, 2020).

Findings

Guidelines

No North American professional guidelines currently address transperineal laser ablation of the prostate for benign prostatic hyperplasia.

An interventional procedures guidance from the National Institute for Health and Care Excellence recommends transperineal laser ablation to treat lower urinary tract symptoms of benign prostatic hyperplasia in people who

cannot have transurethral resection of the prostate or other transurethral procedures, and only with special arrangements for clinical governance, consent, and audit or research. In people who can have transurethral resection of the prostate or other transurethral procedures, more research is needed on the transperineal approach (National Institute for Health and Care Excellence, 2025).

Evidence review

The evidence of safety and effectiveness is summarized in two systematic reviews (Alberti, 2025, n = 702; Altieri, 2025; n = 717). The body of evidence included in these reviews consists of two small, randomized controlled trials comparing two prostate procedures — transperineal laser ablation and transurethral resection (Bertolo, 2023; Canat, 2023) — and several small, observational studies, each associated with a moderate-to-high risk of bias. One additional randomized controlled trial compared transperineal laser ablation to transurethral water vapor thermal therapy (Pacini, 2025; Zucchi, 2025). In all studies, the transperineal laser ablation procedure was performed with the EchoLaser X4 system.

Transperineal laser ablation is safe and feasible for relieving obstructive lower urinary tract symptoms, while sparing overall sexual function. Complication rates varied widely in individual studies, ranging from 0% to 65%. The most common complications were low-grade and transient (mainly Clavien-Dindo Grades I and II), such as transient dysuria and hematuria, hematospermia, urinary tract infections, and a few cases of acute urinary retention. No major complications were reported. Most patients were discharged on the same day, after a short post-operative observation period. Recovery was rapid, and while most studies had short follow-up periods, a few studies reported maintaining treatment effects up to a median of 12 months (Alberti, 2025; Altieri, 2025).

In the three small, randomized controlled trials directly comparing transperineal laser ablation to other transurethral procedures, the study populations represented participants mostly in their mid-sixties with severe lower urinary tract symptoms, obstructed urine flow, and mild to moderate erectile dysfunction impacting quality of life (Bertolo, 2023, n = 51; Canat, 2023, n = 25; Pacini, 2025 and Zucchi, 2025, both n = 80). Transperineal laser ablation provided significant short-term improvement in uroflow measurements, symptoms, and quality of life without compromising erectile or ejaculatory function and with a low risk of complications, while transurethral resection of the prostate offered superior improvement in uroflow measures but at a greater risk to sexual function (Bertolo, 2023; Canat, 2023). Compared to transurethral water vapor thermal therapy, transperineal laser ablation demonstrated comparable uroflow outcomes without compromising sexual function but slightly superior symptom resolution and quality of life improvement (Pacini, 2025; Zucchi, 2025).

There is no consensus on which patients would most benefit from this procedure, as there were no standardized inclusion criteria. Most study participants had medical therapy with no wash-out period before the procedure, and studies included those eligible and ineligible for transurethral resection of the prostate. Median/mean age varied widely, as did median/mean prostate volumes (ranging from 38 cc to 102 cc across studies). Studies were inconsistent in excluding patients with an obstructive median lobe or indwelling/intermittent catheters, although patients with anatomical or functional alterations that can impact bladder function or with a history of rectal surgery were generally excluded. Studies showed high heterogeneity (I^2 > 85% for most outcomes), suggesting considerable variability in the treatment effects across studies (Alberti, 2025; Altieri, 2025).

According to the systematic review investigators, the patients most likely to benefit appear to be those with medium-sized prostates who want to relieve obstructive symptoms without compromising sexual function and those who wish to avoid the risks associated with general anesthesia and hospitalization. Further research is needed to address long-term effectiveness and the patient-specific or intervention-related factors contributing to the variability in outcomes. This information will provide more robust findings that are comparable in quality to the evidence supporting resection or enucleation procedures considered the standard of care (Alberti, 2025; Altieri, 2025).

Two registry studies are in progress to assess long-term outcomes, with follow-up periods of five years. The estimated completion dates are January 2034 (ClinicalTrials.gov identifier NCT06564415) and February 2029 (ClinicalTrials.gov identifier NCT03776006).

References

On 8/7/2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “prostatic hyperplasia” (MeSH), “laser therapy” (MeSH), “Lower Urinary Tract Symptoms/surgery” (MAJR), “transperineal laser ablation,” “SoracteLite,” “transperineal laser ablation,” and “prostate.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Alberti A, Lo Re M, Nicoletti R, et al. Transperineal laser ablation in the management of benign prostatic hyperplasia: An updated systematic review and pooled analysis. *Prostate Cancer Prostatic Dis*. 2025. Doi: 10.1038/s41391-025-00952-1.

Altieri VM, Di Bello F, Saldutto P, et al. Outcomes and safety of trans perineal laser ablation of the prostate: A systematic review. *World J Urol*. 2025;43(1):385. Doi: 10.1007/s00345-025-05753-8.

Bertolo R, Iacovelli V, Cipriani C, et al. Ejaculatory function following transperineal laser ablation vs TURP for benign prostatic obstruction: A randomized trial. *BJU Int*. 2023;132(1):100-108. Doi: 10.1111/bju.16008.

Canat HL, Gurbuz C, Bozkurt M. Transurethral resection of the prostate (TURP) versus transperineal laser ablation (TPLA) due to benign prostatic hyperplasia (BPH): Prospective and comparative study. *Int Urol Nephrol*. 2023;55(11):2747-2752. Doi: 10.1007/s11255-023-03717-8.

ClinicalTrials.gov. European registry for transperineal laser ablation of prostate (TPLA) for lower urinary tract symptoms. ClinicalTrials.gov identifier NCT06564415. https://www.clinicaltrials.gov/study/NCT06564415?intr=TPLA&aggFilters=status:rec%20not&rank=3 . Estimated study completion January 2034. Last update posted August 21, 2024.

ClinicalTrials.gov. Registry: TPLA for LUTS. ClinicalTrials.gov identifier NCT03776006. https://www.clinicaltrials.gov/study/NCT03776006?term=NCT03776006&rank=1. Estimated study completion date February 1, 2029. Last update posted January 18, 2019.

Elasta-echolaser SpA. Soractelite. https://www.elesta-echolaser.com/soractelite/?lang=en. Published 2020.

Lerner LB, Barry MJ, Das AK, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline. Unabridged version. American Urological Association. https://www.auanet.org/documents/Guidelines/PDF/2023%20Guidelines/BPH%20Unabridged%2002-20-24%20Final.pdf. Last updated 2023.

National Institute for Health and Care Excellence. Transperineal laser ablation for treating lower urinary tract symptoms of benign prostatic hyperplasia. *Interventional procedures guidance.* Reference number: IPG798. https://www.nice.org.uk/guidance/ipg798. Published January 8, 2025.

Ng M, Leslie SW, Baradhi KM. Benign Prostatic Hyperplasia. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK558920/. Last updated October 20, 2024.

Pacini M, Zucchi A, Salonia A, et al. Short term results after minimally invasive treatments for benign prostatic enlargement: The first randomized trial comparing transperineal laser ablation and water vapor ablation. *Prostate Cancer Prostatic Dis*. 2025. Doi: 10.1038/s41391-025-00972-x.

Sessa F, Bisegna C, Polverino P, et al. Transperineal laser ablation of the prostate (TPLA) for selected patients with lower urinary tract symptoms due to benign prostatic obstruction: A step-by-step guide. *Urology Video Journal*. 2022;15:100167. https://doi.org/10.1016/j.urolvj.2022.100167.

U.S. Food and Drug Administration. 510(k) premarket approval of Echolaser X4 to El. En Electronic Engineering Spa % Paolo Peruzzi. K181510. https://www.accessdata.fda.gov/cdrh_docs/pdf18/K181510.pdf. Dated September 4, 2018.

U.S. Food and Drug Administration. 510(k) premarket approval of Echolaser X4 to Elesta Spa % Maurizio Pantaleoni. K213594. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K213594. Dated May 3, 2022.

Zucchi A, Bartoletti R, Antonov P, et al. Preserving erectile and ejaculatory function in patients undergoing minimally invasive techniques: The first randomized clinical trial comparing convective water vapor ablation and transperineal laser ablation. *J Sex Med*. 2025;22(8):1447-1454. Doi: 10.1093/jsxmed/qdaf150.

Policy updates

9/30/2025 initial review date and clinical policy effective date: [ccp.04_effective_date]

ZOLL Heart Failure Management System

Clinical Policy ID: CCP.1547

Recent review date: 7/31/2025

Next review date: 11/30/2026

Policy contains: Heart failure; pulmonary edema; remote monitoring; µCor; ZOLL Heart Failure Management System.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies, along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation, are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

The ZOLL® Heart Failure Management System (ZOLL Manufacturing Corporation, San Jose, California) is investigational/not clinically proven and, therefore, not medically necessary.

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Guideline-directed care for heart failure.

Background

Heart failure, also called congestive heart failure, occurs when the heart cannot pump enough blood and oxygen to support other body organs. This can result from any structural or functional impairment of ventricular filling or pumping. Heart failure is a leading cause of morbidity and mortality and a substantial burden to health care systems. Racial and ethnic disparities in heart failure-related mortality persist, with non-Hispanic Black patients having the highest death rate per capita (Heidenreich, 2022).

Heart failure is defined clinically in several ways. The American College of Cardiology/American Heart Association's four stages emphasize the development and progression of disease in which advanced stages are associated with reduced survival. The New York Heart Association Classification characterizes patient symptoms and functional capacity, is an independent predictor of mortality, and is used to determine treatment eligibility. Left ventricular ejection fraction reflects differing prognosis and response to treatments and has been used to determine clinical trial eligibility (Heidenreich, 2022).

In the United States, an estimated 6.7 million people live with heart failure. Its prevalence is projected to increase further, affecting more than eight million adults age 18 years and older by 2030 (Martin, 2025). Initial hospitalizations and rehospitalizations (30- and 90-day) account for the largest component of direct medical costs attributed to heart failure diagnoses (Osenenko, 2022).

Current methods to reduce decompensation leading to heart failure hospitalizations include frequent weight monitoring, blood pressure measurements, Holter monitoring, and telehealth platforms for structured assessment of symptoms. However, these methods often reflect later changes in decompensation and are time-consuming and resource-intensive. Remote monitoring devices, broadly categorized as implantable or less invasive wearable options, have been developed to detect impending signs of heart failure decompensation and reduce heart failure hospitalization (Kobe, 2023).

The ZOLL Heart Failure Management System, formerly the μCor Heart Failure and Arrhythmia Management System, is a wearable, patch-based sensor that uses radiofrequency technology to measure the Thoracic Fluid Index for early detection of changes in pulmonary fluid levels. It is intended to continuously record, store, and transmit thoracic fluid data along with heart rate, respiratory rate, activity, posture, and heart rhythm. The U.S. Food and Drug Administration issued 510(k) premarket approval intended for patients who are 21 years of age or older who require either monitoring for the detection of non-lethal cardiac arrhythmia (including, but not limited to, atrial fibrillation, atrial flutter, ventricular ectopy, and bradyarrhythmia) or monitoring fluid management (U.S. Food and Drug Administration, 2018).

Findings

Guidelines

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guideline for the management of heart failure does not address the use of non-invasive wireless technology to monitor pulmonary fluid levels as an early indicator for heart failure decompensation or arrhythmia detection (Heidenreich, 2022).

A scientific statement by the Heart Failure Society of America lists the ZOLL Heart Failure Management System (herein called "ZOLL") among a number of device-based therapies under investigation that may address an unmet need in the future (Estep, 2024).

Evidence review

The evidence of the effectiveness of the ZOLL device to track pulmonary edema is limited to two validation studies and one concurrent-control trial. While there is an unmet need for early detection of heart failure decompensation to avoid heart failure hospitalization, there is insufficient evidence documenting long-term outcomes and who would most benefit from this technology (e.g., those with or without associated pulmonary edema or on diuretic therapy).

Early validation studies analyzed the ability of the μCor Heart Failure and Arrhythmia Management System to measure a patient's fluid status. In 20 participants with end-stage kidney disease with or without heart failure, 17 exhibited very strong or strong correlations (Pearson's correlation coefficient $r \geq 0.7$) between μCor thoracic fluid measurement and total body fluid removal during dialysis (Connaire, 2020; ClinicalTrials.gov identifier NCT03072732). In another trial of 66 inpatients recently admitted with acute heart failure (predominantly New York Heart Association functional class III to IV) and 54 healthy or stable controls, the diagnostic performances of μCor and computed tomography were similar: sensitivity 70% versus 86%; specificity 82% versus 83%; positive predictive value 82% versus 86%; negative predictive value 69% versus 83%, respectively, and correlation was strong ($r = 0.7$, $P < .001$) (Wheatley-Guy, 2020).

The evidence of clinical benefit is limited to one manufacturer-sponsored, multicenter, prospective, concurrent-control trial (Boehmer, 2024). The control arm (n = 245) was labeled Benefits of Microcor in Ambulatory Decompensated Heart Failure (BMAD-HF), ClinicalTrials.gov identifier NCT03476187), and the intervention arm (n = 249) was labeled Benefits of Microcor in Ambulatory Decompensated Heart Failure (BMAD-TX; ClinicalTrials.gov identifier NCT04096040). The study enrolled participants who had a recent hospitalization within 10 days for heart failure and a heart failure event within the previous six months. Participants in the intervention arm wore the ZOLL patch continuously for 90 days. Using intention-to-treat analysis, the primary endpoint was time to first heart failure hospitalization. Secondary endpoints included a composite heart failure-related events (emergency department visits, hospitalizations, and death) and quality of life as measured with the 12-item Kansas City Cardiomyopathy Questionnaire.

Compared with the control arm, participants using ZOLL lung fluid monitoring had a 37% reduction in heart failure hospitalization (hazard ratio = 0.63, $P = .03$, absolute reduction = 7%), a 38% reduction in the composite outcome of heart failure events ($P = .02$, absolute reduction = 9%), and clinically meaningful improvement in quality of life (12 points higher, $P = .004$). Study limitations included a short follow-up period, lack of randomization, a non-blinded intervention arm, and small but significant baseline differences in the use of angiotensin receptor–neprilysin and sodium glucose cotransporter 2 inhibitors between arms. The effects of COVID-19 on remote management considerations, presence of pulmonary congestion at enrollment, and need for diuretic agents are unclear (Boehmer, 2024).

Extrapolating from the above trial data, Bosworth Smith (2025) estimated ZOLL's cost-effectiveness over a five-year time horizon in the United States context. Compared to the standard of care, an estimated $6,723 reduction in care costs and fewer hospital readmissions (mean, 1.075 versus 1.201 per patient) were projected at five years with ZOLL monitoring. However, there is considerable uncertainty in the model inputs after 90 days, and long-term data are needed to confirm analytical trends.

References

On July 10, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "Monitoring, physiologic" (MeSH), "Heart failure" (MeSH), "remote sensing technology," "μCor," "ZOLL," and "heart failure management system." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-

analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Boehmer JP, Cremer S, Abo-Auda WS, et al. Impact of a novel wearable sensor on heart failure rehospitalization: An open-label concurrent-control clinical trial. *JACC Heart Fail*. 2024;12(12):2011-2022. Doi: 10.1016/j.jchf.2024.07.022.

Bosworth Smith A, Silas U, Veloz A, et al. Cost-effectiveness analysis of a heart failure management system in the United States. *J Health Econ Outcomes Res*. 2025;12(1):113-119. Doi: 10.36469/001c.130066.

Connaire JJ, Sundermann ML, Perumal R, Herzog CA. A novel radiofrequency device to monitor changes in pulmonary fluid in dialysis patients. *Med Devices (Auckl)*. 2020;13:377-383. Doi: 10.2147/mder.S277159.

Estep JD, Salah HM, Kapadia SR, et al. HFSA scientific statement: Update on device based therapies in heart failure. *J Card Fail*. 2024;30(11):1472-1488. Doi: 10.1016/j.cardfail.2024.07.007.

Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation*. 2022;145(18):e895-e1032. Doi: 10.1161/cir.0000000000001063.

Kobe EA, McVeigh T, Hameed I, Fudim M. Heart failure remote monitoring: A review and implementation how-to. *J Clin Med*. 2023;12(19):6200. Doi: 10.3390/jcm12196200.

Osenenko KM, Kuti E, Deighton AM, Pimple P, Szabo SM. Burden of hospitalization for heart failure in the United States: A systematic literature review. *J Manag Care Spec Pharm*. 2022;28(2):157-167. Doi: 10.18553/jmcp.2022.28.2.157.

U.S. Food and Drug Administration. 510(k) approval letter to ZOLL Manufacturing Corporation. K172510. Trade/Device Name: µCor Heart Failure and Arrhythmia Management System. https://www.accessdata.fda.gov/cdrh_docs/pdf17/K172510.pdf. Dated May 11, 2018.

Wheatley-Guy CM, Sajgalik P, Cierzan BS, Wentz RJ, Johnson BD. Validation of radiofrequency determined lung fluid using thoracic CT: Findings in acute decompensated heart failure patients. *Int J Cardiol Heart Vasc*. 2020;30:100645. Doi: 10.1016/j.ijcha.2020.100645.

Policy updates

7/31/2025 initial review date and clinical policy effective date: [ccp.04_effective_date]