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ABSTRACT

A systematic review with semi-quantitative synthesis and GRADE qualification of the effectiveness of a keratin-based matrix in treating hard-to-heal wounds

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Abstract

Background: Hard-to-heal wounds impose substantial morbidity, cost, and, in the case of diabetic foot ulcers, elevated mortality risk. Venous leg ulcers (VLUs) and variants of epidermolysis bullosa (EB) likewise impose major chronic-disease burden and healthcare cost. Keratin biomaterials derived from wool have demonstrated regenerative potential by stimulating keratinocyte activation and collagen synthesis.

Objective: To systematically assess the clinical efficacy and certainty of evidence for a wool-derived keratin-based matrix (KBM) (Keramatrix [Q4165], Biowound Solutions Inc., Las Vegas, NV, USA), a 510(k) U.S. Food and Drug Administration (FDA) approved product with cleared indications, and related keratin biomaterials in the management of hard-to-heal wounds, using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Methods: Literature from 2006–2025, including a randomized controlled trial (RCT), prospective cohorts, and case-series data, was extracted into a master evidence table. Studies were assessed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) and evaluated across five GRADE domains with appropriate downgrading and upgrading factors. Data were synthesized narratively and semi-quantitatively, with directional summaries of epithelialization and closure outcomes rather than formal meta-analytic pooling due to heterogeneity among studies.

Results: Thirty-two studies (n≈700 human wounds) were identified: one RCT (High certainty), six comparative or cohort studies (Moderate), fifteen case series, and ten case reports or preclinical studies (Low–Very Low). Across seven comparative studies (n≈400 wounds), keratin-based matrix (KBM) treated groups achieved 60–80 % complete or ≥ 50 %

partial closure by 8–12 weeks versus 25–40 % among controls (approximate RR 1.97; 95 % CI 1.2–3.2). This finding, based on a fixed-effect inverse-variance summary of study-level risk ratios, reflects a semi-quantitative directional effect rather than a formal meta-analysis. Owing to heterogeneity of endpoints, this estimate is reported as a semi-quantitative directional effect rather than a formal meta-analysis. Uncontrolled series reported similar healing rates in treated wounds without formal comparators. No serious adverse events were reported.
Conclusion: Using formal GRADE qualification, the KBM used in these studies demonstrate consistent clinical efficacy and favorable safety across diabetic foot ulcers, venous leg ulcers, and epidermolysis bullosa. Evidence certainty is moderate overall, driven by one high-certainty RCT and multiple concordant cohort studies. The findings support CMS formulary inclusion of Keramatrix as a reasonable and necessary adjunctive therapy following failure of standard of care techniques. Ongoing real-world data continue to corroborate and expand these findings across diverse care settings.

Certainty of Evidence: Overall Moderate.
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