Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

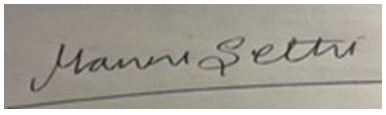
Plan: AmeriHealth Caritas Pennsylvania & Keystone First	Submission Date:11/1/2025
Policy Number: CCP.1532	Effective Date:11/1/2023 Revision Date:10/1/2025
Policy Name: Low-frequency ultrasound therapy for wound management	

Type of Submission:

☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☒ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	Signature of Authorized Individual: 

Keystone First
Family of Health Plans

Low-frequency ultrasound therapy for wound management

Clinical Policy ID: CCP.1532

Recent review date: 10/2025

Next review date: 2/2027

Policy contains: low-frequency ultrasound, MIST system, wound management

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's 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 Keystone First, on a case by case basis, 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. Keystone First's 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. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

Low-frequency ultrasound therapy for wound management is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Advanced wound dressings.
Compression bandaging.
Systemic antibiotic therapy.
Wound debridement.

Background

A wound is a disruption of the normal structure and function of skin and soft tissue, broadly classified as acute or chronic. Acute wounds, such as surgical incisions or traumatic injuries, follow an orderly cascade of hemostasis, inflammation, proliferation, and remodeling (Nagle, 2023). Chronic wounds, by contrast, fail to progress through these phases, often persisting beyond 3 months due to prolonged inflammation, infection, biofilm formation, and dysregulated repair signaling (Demidova-Rice, 2012).

Management of chronic wounds involves therapies designed to reduce bioburden, maintain a healing environment, and stimulate tissue repair. Standard care begins with debridement to remove devitalized tissue and decrease bacterial load, accomplished by surgical, enzymatic, or autolytic methods (Manna, 2023). Adjunctive dressings such as hydrocolloids, foams, and hydrogels help regulate moisture and protect the wound (Zaver, 2023). In selected cases, negative pressure wound therapy supports granulation and edema reduction, while topical growth factors, such as platelet-derived growth factor, target angiogenesis and cellular proliferation (Demidova-Rice, 2012).

Low-frequency ultrasound (LFU), generally delivered at 20–60 kHz, has gained attention as an adjunct for chronic wound care. Proposed mechanisms include biofilm disruption, microstreaming and cavitation effects that facilitate selective debridement, enhanced penetration of topical agents, and modulation of inflammatory pathways (Chang, 2017). Evidence from preclinical and clinical studies suggests potential benefits in wound size reduction and pain control, though methodological limitations and small trial sizes temper conclusions (Chang, 2017).

The MIST Therapy System (Celleration, Inc.) is a noncontact LFU device cleared by the U.S. Food and Drug Administration in 2005 under the 510(k) pathway for wound cleansing and debridement (U.S. Food and Drug Administration, 2005). Delivered through a saline mist, MIST has been evaluated in both clinical and experimental contexts. In clinical series, adjunctive use of MIST accelerated closure of chronic wounds compared to standard care (Ennis, 2006; Kavros, 2008). In a diabetic mouse model, LFU therapy enhanced neovascularization and wound closure (Maan, 2014). These findings support its consideration as a therapeutic option in wound management.

Findings

Across guidelines, systematic reviews, and meta-analyses, the clinical utility of low-frequency ultrasound therapy for wound management appears conditional on wound type and on whether ultrasound assists instead of replaces sharp debridement. Guideline bodies generally advise selective adjunct use at most and recommend against routine use in diabetic foot ulcers, citing small, short, and often unblinded trials with heterogeneous parameters and limited follow-up on complete healing and recurrence. Systematic reviews typically show no advantage over standard care in direct comparisons over 8 to 12 weeks, yet they note signals that concentrate when ultrasound is deployed to augment debridement and when patient selection is explicit. Meta-analyses centered on ultrasound-assisted debridement report higher short-term healing odds within four to 14 weeks, but effect sizes are sensitive to risk of bias, protocol variability which frames the cautious interpretation developed in the sections that follow.

Guidelines

Guideline positions converge on caution. The National Institute for Health and Care Excellence concluded that while the noncontact low-frequency device shows promise in difficult-to-heal wounds, the amount and quality of research are insufficient to support routine adoption; only 2 of 10 cited studies were randomized and just 3 enrolled more than 70 participants, with wound heterogeneity and missing recurrence data further limiting inference (National Institute for Health and Care Excellence, 2011). For arterial ulcers, the Wound Healing Society judged that the lack of randomized trials and variability in study settings preclude support for routine use (Federman, 2016). For venous leg ulcers, the Society advised that ultrasound can be considered when

progress has stalled, but assigned a Level III recommendation because technique, settings, and treatment duration are not established (Marston, 2016).

The Wound Healing Society's 2023 update on pressure ulcers newly states that ultrasound may be useful as an adjunct for pressure ulcers unresponsive to standard therapy, noting reports with nonthermal low-frequency ultrasound and with high-frequency pulsed ultrasound; the recommendation remains Level III because parameters and optimal duration are not defined (Gould, 2024). For diabetic foot ulcers, the International Working Group on the Diabetic Foot advises not to use any form of ultrasonic debridement over standard care (sharp debridement), issuing a strong recommendation based on low-certainty evidence from three randomized trials that were unblinded and showed no difference in complete healing within trial time frames; a small signal for shorter time to healing in one high-risk study does not change the conclusion (Chen, 2023).

Systematic reviews

In venous leg ulcers, a Cochrane review identified two randomized trials over eight to 12 weeks (N = 61) comparing low-frequency ultrasound with no ultrasound and judged the evidence very low quality, with no statistically significant between-group differences in healing (Cullum, 2017). Reviews pooling chronic wound studies emphasize limitations in design and scale. A systematic review of 25 studies (N = 850) found that 21 studies provided low-level evidence and 16 enrolled 20 or fewer patients; four larger studies addressing noncontact low-frequency ultrasound accounted for nearly 60% of all participants, underscoring concentration of the evidence base and the need for larger, better designed trials (Chang, 2017). For diabetic foot ulcers specifically, a focused systematic review comparing low-frequency ultrasonic debridement with nonsurgical sharp debridement synthesized 2 studies (N = 173) and found no difference in the proportion healed (Michailidis, 2018).

In venous leg ulcers, a Cochrane review synthesized 2 randomized trials over 8 to 12 weeks (N = 61) that compared low-frequency ultrasound with no ultrasound and found very low-quality evidence with no statistically significant difference in healing between groups (Cullum, 2017). A focused review comparing low-frequency ultrasonic debridement with nonsurgical sharp debridement in diabetic foot ulcers synthesized 2 studies (N = 173) and found no difference in the proportion healed, indicating no replacement advantage for ultrasonic debridement when standard sharp debridement is available (Michailidis, 2018). A broader systematic review of chronic wounds included 25 studies (N = 850), noted that 4 studies on noncontact low-frequency ultrasound accounted for nearly 60% of all participants, and concluded that 21 of 25 studies were low-level evidence and 16 had 20 or fewer patients, which underscores the need for adequately powered trials with standardized protocols (Chang, 2017). Taken together, these reviews favor reserving ultrasound for adjunctive roles and reinforce that quality of debridement, patient selection, and concomitant standard care determine outcomes more than device choice alone.

Narrative reviews that survey technique and implementation issues reach convergent conclusions. A clinical review argued that ultrasound is superior to standard care for wound debridement in some settings, while findings comparing low-level and high-level ultrasound remain mixed, and it highlighted persistent barriers such as absence of standardized treatment protocols and limits to trial design that impede generalizability (Kavros, 2018). A broader review of physical therapies reported that low-frequency ultrasound at 30 to 40 kilohertz has been applied with favorable results in leg ulcers, typically delivered to peri-wound skin for 5 to 10 minutes with a coupling gel, and noted Food and Drug Administration clearance as an adjuvant therapy for wound healing (Fernández-Guarino, 2023). That review also emphasized the paucity of clinical studies outside leg ulcers and the need for additional randomized trials with defined dosing, schedules, and follow up on complete healing

and recurrence (Fernández-Guarino, 2023). Integrating these narrative reviews with the quantitative evidence above suggests that any incremental benefit likely depends on disciplined protocolization and explicit patient selection rather than device brand or nominal frequency alone.

Meta-analyses

Earlier meta-analytic work pooling mixed chronic wound populations suggested short-term advantages but with substantial bias concerns. A review that included 8 randomized trials reported improved outcomes within approximately 5 months of treatment; within the sham-controlled subset of 2 trials (N = 77), the proportion of nonhealed wounds by 3 months was lower with ultrasound, though high risk of bias and heterogeneity limit confidence in the magnitude and durability of effect (Voigt, 2011). Findings from an individual, double-blind, randomized trial in neuropathic diabetic foot ulcers over 28 days (n = 60) are consistent with early within-study area reduction signals, with 97.1% versus 73.1% achieving at least 50% reduction from baseline under active versus sham treatment (Rastogi, 2019).

More recent evidence targeted to ultrasound-assisted debridement in diabetic foot ulcers synthesized 11 randomized controlled trials (N = 696) across 6 countries and found higher odds of complete healing within 4 to 14 weeks for ultrasound-assisted debridement versus standard approaches, with reported odds ratio 2.60 (95% confidence interval 1.67 to 4.03) and supportive improvements in wound area and granulation; serious adverse events were not increased. Protocols, frequencies, and treatment schedules varied, and many trials were unblinded, which constrains applicability and certainty (Liu, 2024).

In 2025, we redrafted the background section and reorganized the findings section and added new evidence from recent guideline updates (Chen, 2023; Gould, 2024) and a new meta-analysis (Liu, 2024). No policy changes warranted.

References

On September 14, 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 “low-frequency ultrasound,” “MIST system,” and “wound management.” 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.

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Policy updates

10/2023: initial review date and clinical policy effective date: 11/2023

10/2024: Policy references updated.

10/2025: Policy references updated.