

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)	
Effective Date: 6/1/2020  <div style="text-align: right;">6/1/2020</div>	Section: MED	Policy No: 379
	Technology Assessment Committee Approved Date: 8/11; 7/12; 12/13; 12/14; 10/15 Medical Policy Committee Approved Date: 9/16; 11/17; 12/18; 3/19; 3/2020, 5/2020	
Medical Officer	Date	

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayn Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

Non-contact wound therapy, including low frequency ultrasound wound therapy and normothermic wound therapy, is considered **investigational and is not covered.**

Link to [Policy Summary](#)

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
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CPT/HCPCS CODES

All Lines of Business Except Medicare	
Not covered	
97610	Low frequency, non-contact, non-thermal ultrasound, including topical application(s), when performed, wound assessment, and instruction(s) for ongoing care, per day
A6000	Non-contact wound warming wound cover for use with the non-contact wound warming device and warming card
E0231	Non-contact wound warming device (temperature control unit, ac adapter and power cord) for use with warming card and wound cover.
E0232	Warming card for use with the non contact wound warming device and non contact wound warming wound cover

DESCRIPTION

Low-Frequency Ultrasound Therapy

Non-contact, low-frequency ultrasound therapy (i.e. Mist Therapy™ System) has been marketed to provide cleansing and debridement of wounds. Treatment with this device involves holding an ultrasonic handset 1 cm away from the wound and applying a saline solution to the handset, generating a saline mist that is designed to carry low levels of ultrasonic energy into the wound. According to the device manufacturer, this treatment promotes healing of acute, traumatic, and chronic wounds by stimulating cellular activities that contribute to healing and by cleaning the wound surface. Under normal circumstances, patients undergo Mist Therapy on an outpatient basis in 3 sessions per week and 3 to 12 minutes of treatment per session, depending on wound size.

Noncontact Normothermic Wound Therapy

Noncontact normothermic wound therapy utilizes a noncontact wound cover and a warming unit to maintain humidity and produce normothermia at the wound site. It is hypothesized that increasing the wound temperature promotes healing by increasing blood flow and oxidation in the wound, which in turn increases collagen deposition, scar formation, and antibacterial processes.¹

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of non-contact low frequency ultrasound treatment of wounds. Below is a summary of the available evidence identified through March 2020.

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
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Low-Frequency Ultrasound Therapy

Systematic Reviews

- In 2016 (updated 2018), Hayes evaluated MIST Therapy System for the treatment of lower extremity, arterial and diabetic foot ulcers. In total, 4 studies were included for review (3 RCTs, 1 retrospective cohort study).² Sample sizes ranged from 12 to 210 patients and follow up varied from 5 weeks to 6 months.

Compared with patients receiving standard care alone, 3 studies (1 judged to be “fair-quality”, 2 judged to be “poor-quality”) reported significant improvements in wound reduction and healing among patients receiving MIST. One poor-quality, retrospective cohort study reported improvements in wound healing between treatment and control arms, but no significant differences in outcomes by wound categories. One RCT also reported that patients receiving MIST 3 times per week experienced better wound outcomes than patients receiving MIST either once a week, or standard care without MIST.

Hayes determined the overall body of evidence to be of “low quality.” Despite positive results, limitations of the individual studies included small sample sizes, inadequate follow-up, lack of assessor blinding, retrospective study design of 1 study, patient attrition, a lack of power analysis and limited reporting of safety outcomes. Hayes assigned a “C” rating to MIST when used as an adjunct to standard wound care for lower extremity arterial wounds or diabetic foot ulcers, noting “substantial uncertainty [of efficacy]...due to a lack of adequately powered studies with sufficient follow-up.”²

- In 2016 (updated 2018), Hayes conducted an evidence review evaluating MIST Therapy System for the treatment of venous leg ulcers (VLUs).³ In total, 5 clinical studies (4 RCTs, 1 retrospective cohort study) were reviewed. Sample sizes varied from 36 to 210, and follow-up ranged from 11 weeks to 6 months after complete wound healing.

Compared to patients receiving standard wound care (SWC) alone or SWC plus high-frequency ultrasound (HFU), one fair-quality RCT reported significant reductions in wound size and wound pain, and fewer patients with severe edema and among patients receiving MIST plus SWC. A second RCT reported significant improvements at 4-week follow-up in pain scores, and mean percentage of ulcer area in patients receiving MIST plus SWC compared to patients receiving SWC alone. A third RCT reported no significant differences between treatment and control groups in ulcer changes, pain, quality of life or adverse events. Lastly, a retrospective cohort study reported faster healing rates in all wounds among patients receiving MIST plus SWC. In sum, four of the reviewed studies (3 “fair quality” RCT’s and one “poor quality” cohort study) reported a significant increase in wound reduction and healing in patients receiving MIST plus SWC. One study did not report significant increase in wound reduction and healing.

Hayes assessed the overall body of evidence to be of “moderate-quality,” suggesting that MIST, when used alongside SWC, demonstrated potential to improve healing relative to SWC alone.

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
-----------------------	--

However, results' generalizability was limited by studies' small sample size, inadequate follow-up, lack of power analyses, retrospective design (1 study), lack of blinding of outcome assessors and heterogeneous treatment parameters. Hayes assigned MIST a "C" rating as an adjunct to SWC for VLUs. Hayes concluded that "additional randomized controlled trials of sufficient power ...are needed to make definitive conclusions regarding the safety and long-term effectiveness of noncontact low frequency ultrasound with the MIST Therapy System."³

- In 2017, Cochrane published a systematic review of evidence evaluating the use of high- and low-frequency ultrasound (HFU and LFU) technologies for the treatment of venous leg ulcers.⁴ Two independent reviewers searched the literature through September 2016, systematically identified eligible studies, assessed quality, and extracted data. Primary outcomes of interest were time to complete wound healing and frequency of complete healing. Secondary outcomes included health-related quality of life, adverse events and cost.

In total, 11 trials were included for review (7 assessing HFU and 2 trials assessing LFU (n=61)), of which 10 were assessed to be at an "unclear or high risk of bias." Both trials that assessed LFU applied LFU three times a week via water bath. Using a fixed-effect model, Cochrane investigators pooled results from these two studies and found no clear difference between treatment and control groups (RR 3.91, 95% CI 0.47 to 32.85). As only 3 ulcers were assessed across the two studies, investigators judged the evidence to be insufficient due to a high risk of bias and imprecision. Investigators concluded that "it is uncertain whether therapeutic ultrasound (either high or low frequency) improves the healing of venous leg ulcers."⁴

- In 2017, Chang and colleagues conducted a systematic review of studies evaluating low-frequency ultrasound debridement (LFUD) in the treatment of chronic wounds (LFUD).⁵ Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. In total, 25 studies were included for review. Among included studies, sample sizes ranged from 1 to 133 and follow-up varied from 2 weeks to 18 months. The outcomes of interest were optimal treatment parameters (e.g. ultrasound frequency, treatment time, intervals, and frequency of debridement). Results from reviewed studies indicated that LFUD appeared to work best when used 3 times a week and when shown potentially capable of dispersing biofilms, and decreasing exudate and slough.

Investigators assessed the majority of studies (21 of 25) to represent no higher than level 3 evidence, largely due to study design. Few well-designed clinical trials were retrieved in investigators' searches. Moreover, meta-analysis of results was not possible due to the heterogeneity in studies' design, intervention(s) and outcome measure(s). Investigators concluded that "ultrasound debridement has a role to play in wound care, but [that] elucidating its mechanism of action, effect on biofilms, and treatment parameters for debridement and post-debridement are part of the current research trajectory."⁵

- In 2016, Alkahtani and colleagues conducted a systematic review of 40 studies evaluating ultrasound-based techniques in the treatment of chronic wounds.⁶ Independent investigators searched the literature through May 2017 (including animal and *in vitro* studies), identified eligible studies, and extracted data. Among RCTs reviewed, improvements were reported among in patients

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
-----------------------	--

receiving LFU alongside standard care for the treatment of purulent wounds. However, investigators did not conduct statistical analyses of pooled results. Investigators noted that studies evaluating LFU for the treatment of diabetic wounds lacked strong evidence due to small sample sizes, inadequate follow-up, incomplete randomization, incomplete blinding and the potential for confounding from concurrent interventions. Investigators concluded that additional, larger controlled trials were necessary to establish the both efficacy of LFU and optimal treatment parameters.

- In 2016, ECRI reviewed abstracts of publications evaluating MIST Therapy System for healing chronic wounds.⁷ ECRI searched the literature according to pre-defined criteria through November 2016, and included 13 publications for review.

For the use of MIST in the treatment of venous leg ulcers (n=277), one RCT reported superior wound reduction after 4 weeks for patients receiving MIST compared to patients receiving standard care (62% vs. 45%). A second RCT concluded that wounds treated with MIST healed two months earlier than those treated with standard of care. A third RCT reported ≥50% reduction in wound volume at 12-week follow-up among 63% of wounds treated with MIST versus 29% treated with standard of care. Results from a fourth RCT (n=36) found no difference between MIST and standard of care. For MIST in the treatment of diabetic foot ulcers (n=77), one RCT reported that wound closure at 12 weeks was 41% with MIST, versus 14% with sham MIST. Evidence was insufficient to determine MIST’s efficacy for the treatment of pressure ulcer wounds.

This review was limited by its lack of full-text review. Nonetheless, the literature search was thorough and informative in that no studies comparing MIST to wound care technologies other than standard of care were retrieved. ECRI concluded that “additional RCTs are needed that make appropriate comparisons and report results separately for each chronic wound type.”⁷

Randomized Controlled Trials

- In 2017, Murphy and colleagues conducted an RCT evaluating low-frequency contact ultrasound debridement (LFCUD) on lower extremity wound healing for patients with vascular disease.⁸ In total, 70 patients were randomized to receive LFCUD plus usual care (n=33) or usual care alone (n=37) during 4 weekly visits. Follow-up for the 68 patients who completed the study was 3 months. Outcomes of interest were closed wounds, change in wound surface area (WSA), and wound appearance by the revised Photographic Wound Assessment Tool (revPWAT). Compared to patients receiving usual care only, patients receiving weekly LFCUD treatments had significantly better wound appearance, and WSA ($p = <0.05$); as well as more healed wounds (OR 5.00, 95% CI 1.24-20.25) and fewer instance of wound deterioration.

Limitations include the study’s small sample size, short follow-up, and the lack of a control group receiving sham ultrasound therapy. There was a proportionally higher rate of missed appointments in patients assigned to usual care, which investigators attribute to patients’ lack of blinding. Differing etiologies of patients’ wounds may have similarly confounded results. Moreover, while conditions between treatment and control groups were similar, they were not identical: patients received varying and concurrent wound therapies, potentially affected healing outcomes.⁸

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
-----------------------	--

- In 2019, Rastogi and colleagues conducted a randomized, double-blind, sham-controlled study on low-frequency, noncontact airborne ultrasound therapy for neuropathic diabetic foot ulcers.⁹ Fifty-eight patients were randomized to therapy with an ultrasound device or sham device for 28 days. At 4 weeks, a >50% reduction in wound area was observed in 97.1% of patients in the ultrasounds group and 73.1% in the sham group (P=0.042).

This study was limited due to a small sample size amassed from a single institute and a short follow-up of 4 weeks in which the investigators could not capture the time until participant wounds fully healed. The primary endpoint of percentage of participants with >50% decrease in ulcer area is an unvalidated, surrogate outcome that may inaccurately measure efficacy. Wound areas were smaller for sham group at baseline compared to the ultrasound group (11.3 ± 8.2 cm² and 14.8 ± 13.8 cm²). While ulcer areas noticeably reduced from baseline to week 1 for the ultrasound group compared to the sham group, the change in area was almost equal between week 2, 3, and 4. Final measurements were 3.2 cm² and 3.5 cm² for ultrasound and sham groups. Similarly, baseline data show that wound duration was longer for the sham group than the ultrasound group (15.8 ± 11.2 and 12.1 ± 10.9 weeks). While these differences were not shown to be statistically significant, the few week difference may favor the ultrasound group. Having a wound for a longer period of time may be due to the fact the wound is slower to heal, suggesting that the control group had wounds that took longer to heal. Overall, the study is of poor quality and does not add to data supporting the use of low-frequency, noncontact ultrasound therapy.

Noncontact Normothermic Wound Therapy

Systematic Reviews

In 2018, Yue and colleagues published a systematic review of RCTs evaluating local warming therapy (LWT) for the treatment of chronic wounds (e.g. pressure ulcers, venous ulcer, arterial ulcers and diabetic foot ulcers). Two independent investigators searched the literature through March 2017 and found no RCTs that met predefined inclusion criteria. Despite the widespread use of LWT to management chronic wounds in many countries, investigators concluded that “the lack of adequate appropriately randomized controlled studies to document [LWT’s] efficacy... is concerning and must be addressed.”¹⁰

CLINICAL PRACTICE GUIDELINES

National Institute for Health and Care Excellence (NICE)

In 2011, NICE stated that “the amount and quality of published evidence on the relative effectiveness of the MIST Therapy system is not sufficient, at the time of writing, to support the case for routine adoption of the MIST Therapy system in the NHS.”¹¹ In 2016, NICE revisited this guideline and decided not to update findings, stating that “new relevant evidence has been published but it is inconclusive and does not fully address the claimed benefits in the scope.”¹²

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
-----------------------	--

Society for Vascular Surgery with American Podiatric Medical Association

In 2016, the Society for Vascular Surgery, in collaboration with the American Podiatric Medical Association, issued joint guidelines on the management of diabetic foot. Ultrasound therapy was not mentioned as a recommended adjuvant option for the treatment of diabetic foot ulcers.¹³

Association for the Advancement of Wound Care (AAWC)

In 2015, the AAWC stated that additional evidence was needed to establish the efficacy of low-frequency ultrasound treatment.¹⁴

Society for Vascular Surgery with American Venous Forum

In 2014, the Society for Vascular Surgery in collaboration with the American Venous Forum issued joint guidelines for the management of venous leg ulcers, and recommended against ultrasound therapy (strength of recommendation: grade 2; quality of evidence: level B).¹⁵

POLICY SUMMARY

Evidence remains insufficient to support the use of non-contact wound therapies (i.e. low-frequency ultrasound therapy, noncontact normothermic wound therapy.) No recent systematic reviews, RCT's or clinical practice guidelines recommend the use of non-contact wound therapies in lieu of, or as an adjunct to standard wound care. Large, high-quality RCTs with adequate follow-up are needed to establish both therapies' long-term safety and efficacy.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
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REGULATORY STATUS

Food and Drug Administration (FDA)

Low-Frequency Ultrasound Therapy

In May 2005, the FDA cleared the MIST Therapy System as a Class II device via the FDA 510(k) process.¹⁶ In August 2012, the MIST 360° Single-Use Applicator Kit, designed to treat larger wounds, received 510(k) clearance.¹⁷ In August 2014, the UltraMIST Therapy System received 510(k) clearance,¹⁸ listing the identical indication for use statement as that listed on the clearance summary for the MIST Therapy System.

Noncontact Normothermic Wound Therapy

Hayes states that Warm-Up Activated Wound Therapy received 510(k) approval from the FDA in March 1997.¹ However, the hyperlink Hayes lists is not functional and a search of relevant FDA databases did not identify pertinent documents.

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

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MEDICAL POLICY	Non-Contact Wound Therapy (All Lines of Business Except Medicare)
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