

# WARMING THERAPY AND ULTRASOUND THERAPY FOR WOUNDS

**Policy Number:** 2018TO521N

**Effective Date:** December 1, 2018

[Instructions for Use](#) ⓘ

Table of Contents	Page
<a href="#">COVERAGE RATIONALE</a> .....	1
<a href="#">APPLICABLE CODES</a> .....	1
<a href="#">DESCRIPTION OF SERVICES</a> .....	1
<a href="#">CLINICAL EVIDENCE</a> .....	2
<a href="#">U.S. FOOD AND DRUG ADMINISTRATION</a> .....	7
<a href="#">CENTERS FOR MEDICARE AND MEDICAID SERVICES</a> .....	7
<a href="#">REFERENCES</a> .....	7
<a href="#">POLICY HISTORY/REVISION INFORMATION</a> .....	9
<a href="#">INSTRUCTIONS FOR USE</a> .....	9

- [Community Plan Policy](#)
- [Warming Therapy and Ultrasound Therapy for Wounds](#)
- [Medicare Advantage Coverage Summary](#)
- [Wound Treatments](#)

## COVERAGE RATIONALE

**Warming therapy or noncontact normothermic wound therapy is unproven and not medical necessary for treating wounds due to insufficient evidence of efficacy.**

**Low frequency ultrasound is unproven and not medically necessary for treating wounds due to insufficient evidence of efficacy.**

## APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
97610	Low frequency, non-contact, non-thermal ultrasound, including topical application(s), when performed, wound assessment, and instruction(s) for ongoing care, per day <i>CPT® is a registered trademark of the American Medical Association</i>

HCPCS Code	Description
A6000	Noncontact wound-warming wound cover for use with the noncontact wound-warming device and warming card
E0231	Noncontact 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 noncontact wound-warming device and noncontact wound warming-wound cover

## DESCRIPTION OF SERVICES

Warming therapy or noncontact normothermic wound therapy uses a noncontact wound cover and a warming unit to apply radiant heat and maintain 100% relative humidity in a wound. The intent is to raise the wound temperature to increase blood flow and oxygen to the wound.

Low frequency or low energy ultrasound using the Mist Therapy® System has been developed to provide simultaneous 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.

The MIST Therapy® System is a noncontact, low-frequency ultrasound debridement device that has been developed to promote healing of chronic wounds by removing yellow slough, tissue exudates, fibrin, and bacteria from the wound surface. The main components of the MIST Therapy® System are an ultrasound generator; a handheld ultrasound transducer; and a single-use, disposable applicator with a bottle reservoir for sterile saline. The transducer tip vibrates 40,000 times per second to generate ultrasound waves at 40 kilohertz (kHz) that are carried to the wound via a saline mist. In addition to wound cleaning, ultrasonic energy has been proposed as a means of stimulating angiogenesis, growth factor production, and other cellular activities that contribute to wound healing (Hayes, 2018).

## CLINICAL EVIDENCE

### **Warming Therapy**

Yue et al. (2018) conducted a systematic review to assess the effects of local warming therapy (LWT) in treating chronic wounds. The inclusion criteria included randomized controlled trials (RCTs) that recruited people with chronic wound(s) (pressure ulcers, venous leg ulcers, arterial ulcers, and diabetic foot ulcers) comparing the effects of LWT with standard wound care or other wound-healing interventions. Primary outcomes included time to healing assessed using appropriate survival analysis, proportion of people with diabetic foot ulcers undergoing amputation of the lower limb at any level, including single toes, and proportion of wounds with complete healing. Secondary outcomes consisted of change in wound size, with change expressed as absolute change or relative change; healing rate; quality of life measured by a validated scale. No RCTs comparing the effects of LWT with standard wound care or other wound-healing interventions amongst people with chronic wound(s) were found. It was not possible to undertake a meta-analysis. The authors concluded that this review highlights the lack of robust evidence for the use of LWT in the treatment of chronic wounds. Thus, no definitive conclusions regarding using LWT for treating chronic wounds can be drawn from this review.

Results of the studies of noncontact normothermic wound therapy (NNWT) for treatment of stage III and IV pressure ulcers and neuropathic ulcers suggest that NNWT, either alone, or in conjunction with standard care and/or offloading, can increase healing rates and the incidence of complete healing (Whitney et al., 2001; Kloth et al., 2002; McCulloch and Knight, 2002; Alvarez et al., 2003). In some cases, these increases were nonsignificant trends, which may reflect the relatively modest treatment effect combined with the small sample sizes. These studies should be interpreted with caution since all of the studies were supported by the manufacturer of the NNWT system, which introduces the possibility of investigator bias. Small study populations, ranging from 17 to 56 wounds per study, lack of blinding, lack of or insufficient statistical analysis and substantial dropout rates further compromised the quality of the evidence. Patient selection criteria were not defined in some studies. Furthermore, long-term follow-up data assessing wound stability and recurrence rates are not available.

In a very small, randomized study evaluating the efficacy of NNWT combined with offloading for treatment of chronic skin wounds associated with osteomyelitis, mean healing time was increased in patients who received NNWT compared with those who received standard care and offloading. However, this difference did not reach statistical significance, and median wound healing times did not differ between groups (Karr, 2003).

Ellis et al. (2003) evaluated 33 patients with full-thickness pressure sores who were randomized to receive standard care or radiant heat therapy with a Warm-Up® device. The Warm-Up® device eradicated bacteria in 6 patients within 2 weeks of starting treatment compared to none in the standard care group. The significance of this study is limited by small sample size.

Forty-one patients with pressure ulcers were randomized to receive radiant heat dressing or hydrocolloid dressing. Fifty-seven percent of the patients using the radiant heat dressing device had complete ulcer healing compared to 44% of the control group. However, the difference was not statistically significant (Thomas et al., 2005).

### **Low Frequency Ultrasound**

Cullum and Liu (2017) performed a systematic review to investigate whether ultrasound helps to heal or improve the symptoms of venous leg ulcers. Eleven randomized controlled trials (RCTs) involving a total of 969 participants were found. Eight studies compared ultrasound with use of no ultrasound for venous leg ulcers and the other three compared ultrasound with sham ultrasound. Seven out of the eleven studies were at high risk of bias, one study was at low risk of bias and bias could not be determine in three studies due to poor reporting. The authors found that the results of one study (337 participants) suggested that high-frequency ultrasound may be associated with more

adverse events such as pain and skin redness (moderate quality evidence). The two studies that evaluated low-frequency ultrasound did not report whether participants experienced side effects. It is also uncertain whether either high- or low frequency ultrasound affects participants' quality of life. The outcomes of adverse effects, quality of life and cost were not reported for low-frequency ultrasound treatment. The authors concluded that it is uncertain whether therapeutic ultrasound (either high or low frequency) improves the healing of venous leg ulcers. They rated most of the evidence as low or very low quality due to risk of bias and imprecision. Most of the studies did not have many participants, had short follow-up times and had poor study design.

A systematic review to examine ultrasound (US) for the treatment of chronic wounds, therapeutic efficacies, and clinical considerations was conducted by Alkahtani et al. (2017). Forty studies were included. The authors found that the evidence for the effectiveness of US for pressure ulcers is limited. Randomized controlled trials conducted showed no significant differences between the treatment groups. Low-frequency US techniques have been used in combination with standard wound care medications for treatment of purulent wounds. The findings of these studies showed the therapeutic effectiveness of US technique as an adjunctive or alternative treatment for purulent wound. Ultrasound to treat diabetic wound studies had a lack of strong evidence due to insufficient sample size, short follow-up period, non-random allocation to treatment arms, non-blinded outcomes evaluation, poor description of control, and concurrent interventions. The review found that therapeutic efficacy of the low-frequency low-dose US technique in chronic venous leg ulcers can shorten the healing period of open wound. The authors concluded that although early studies have been relatively promising, the main challenge for developing US-based techniques as standard treatment options for different wounds is defining an exact dose-response for each wound. Further controlled trials with larger sample sizes are necessary.

Chang et al. (2017) performed a systematic review of current clinical evidence on the use of low-frequency (20-60 kHz) ultrasound in chronic wounds. Twenty-five studies were included. The authors found the current body of evidence supports the use of low frequency ultrasound as adjunctive therapy at least 3 times a week in the treatment of chronic wounds. The majority (21 of 25 studies) of the evidence is limited by study design, representing mostly level 3 to level 5 evidence. One of the major limitations of the study was its inability to discern the efficacy of treatment on different types of wound etiology due to the lack of sufficient study numbers for the pooling of data. More well-designed clinical trials are needed.

A randomized controlled trial was conducted by Murphy et al. (2018) to compare changes in wound size and appearance and health complication rates in patients with vasculopathy and lower-extremity wounds treated with or without low-frequency contact ultrasound debridement (LFCUD). Seventy patients with vasculopathy and lower-extremity wounds of mixed etiology were enrolled in the trial; 68 completed the study. Patients were randomized to receive LFCUD plus usual care (n = 33) or usual care (n = 37) at 4 weekly visits, and were followed for up to 12 weeks. The main outcome measures included closed wounds, change in wound surface area (WSA), and wound appearance by the revised Photographic Wound Assessment Tool (revPWAT). After 4 weekly LFCUD treatments, patients in the LFCUD group had significantly better wound appearance compared with the control group treated only with usual care. LFCUD-treated wounds also had a significant reduction in WSA over 4 weeks that was not found in the usual care group. LFCUD treatment was also associated with a greater number of healed wounds and fewer instances of wound deterioration. The authors concluded that weekly LFCUD applications to patients with significant vasculopathy resulted in superior healing outcomes when compared with current usual wound care practice.

A 2016 ECRI Health Technology Assessment identified and reviewed 13 studies relevant to the Mist Therapy<sup>®</sup> System:

- Diabetic foot ulcers: 2 randomized controlled trials (RCTs) (n = 77)
- Venous leg ulcers: 4 RCTS (n = 277).
- Pressure ulcers: 1 nonrandomized comparison study (n = 85); 1 case series (n = 11).
- Chronic wounds: 1 case series (n = 48); 3 systematic reviews; 1 technology assessment.

The report concluded that the Mist Therapy<sup>®</sup> System shows potential for healing chronic venous leg ulcers and diabetic foot ulcers faster than standard of care. However, available studies are small and do not compare Mist Therapy<sup>®</sup> to other wound care technologies, other than standard care. Evidence is insufficient for drawing conclusions of Mist's effect on pressure ulcers. Additional RCTs are needed that make appropriate comparisons and report results separately for each chronic wound type.

A Hayes Health Technology Brief on the Mist Therapy<sup>®</sup> System reported that a literature search identified 4 studies (n=12 to 210 patients) that evaluated MIST therapy as an adjunct to standard wound care (SWC) for the treatment of diabetic foot ulcers (DFUs) or lower extremity arterial wounds. Overall, a low-quality body of evidence suggests that MIST therapy as an adjunct to SWC may enhance wound healing compared with SWC alone. Three of the studies reported a statistically significant increase in wound reduction and healing when MIST therapy was used. Results from 1 cohort study suggest improvements in wound healing for patients undergoing MIST therapy compared with those undergoing SWC alone; however, no differences were identified between groups when evaluating outcomes by wound categories (ischemic or neuropathic wounds). Limitations of the individual studies include small sample size,

inadequate follow-up, lack of blinding of outcome assessor, retrospective design (1 study), substantial attrition, a lack of power analysis, and limited reporting on safety outcomes (Hayes 2016a; updated 2018).

A Hayes Health Technology Brief for noncontact low-frequency ultrasound using the MIST Therapy System® for treatment of venous leg ulcers literature search identified 5 studies (n=36 to 210 patients) that evaluated MIST therapy as an adjunct to standard wound care (SWC) for the treatment of VLUs. Overall, a moderate-quality body of evidence suggests that MIST Therapy, as an adjunct to SWC, has the potential to enhance VLU healing when compared with SWC alone. Four of the studies reported a statistically significant increase in wound reduction and healing when MIST therapy was added to SWC, while 1 study did not report a statistically significant increase in wound reduction and healing. Limitations of the individual studies include: small sample size, lack of power analyses or lack of sufficient power to detect differences per power analysis, retrospective design (1 study), lack of blinding of outcome assessors, difference in frequency and number of treatments between study groups, lack of analysis of adverse events (AEs), and all of the studies had limited follow-up (Hayes, 2016b; updated 2018).

White et al. (2015) compared non-contact low-frequency ultrasound (NLFU) in addition to standard of care (SOC) 3 times a week, with SOC alone at least once-weekly in a single-site, blinded randomized control trial. Thirty-six randomized patients with chronic venous ulcers completed treatment (17 NLFU + SOC, 19 SOC). NLFU plus SOC patients showed a -47 % change in wound area; SOC, -39 % change; with a difference of -7.4 %. The median number of infections per patient was two in both groups and the change in quality of life (QoL) scores were not significant. Non-contact low-frequency ultrasound plus SOC patients reported a substantial mean reduction in pain score of -14.4 points, SOC patients' pain scores reduced by -5.3; with a difference of -9.1. The authors concluded that the results demonstrated the importance of high-quality wound care and that outcome measures favored NLFU + SOC over SOC, but the differences were not statistically significant. The significance of this study is limited by small sample size and a short follow-up period.

Tricco et al. (2015) examined systematic reviews that focused on interventions to treat complex wounds. Ninety-nine systematic reviews of wound care interventions were included in this overview of systematic reviews; 54 were systematic reviews with meta-analysis results and 45 were systematic reviews without a meta-analysis. Six categories of complex wounds were examined: venous leg ulcers, diabetic foot/leg ulcers, pressure ulcers, mixed arterial/venous leg wounds, unspecified mixed complex wounds and infected surgical wounds. The duration of treatment ranged from 2 days to 160 months and the duration of follow-up ranged from 2 days to 195 months. Based on data from systematic reviews including a meta-analysis with an AMSTAR score  $\geq 8$ , various interventions for complex wounds were identified. These included bandages or stockings (multi-layer, high compression) and wound cleansing for venous leg ulcers; four-layer bandages for mixed arterial/venous leg ulcers; biologics, low frequency, low intensity noncontact ultrasound, and hydrogel dressings for diabetic leg/foot ulcers; hydrocolloid dressings, electrotherapy, air-fluidized beds, and alternate foam mattresses for pressure ulcers; and silver dressings and ultrasound for mixed complex wounds. Moderate to low quality review evidence found topical negative pressure and vacuum-assisted closure could be used for surgical wound infections. The authors concluded that various interventions can be utilized for treatment of varying types of complex wounds, but that few treatments were consistently effective across all outcomes.

A prospective, randomized, controlled, multi-center trial was conducted by Gibbons et al. (2015) to compare percent wound size reduction, proportions healed, pain, and quality-of-life (QOL) outcomes in patients randomized to standard care (SC) alone (n=40) or SC and 40 kHz noncontact, low-frequency ultrasound (NLFU) treatments (n=41) 3 times per week for 4 weeks. One hundred and twelve individuals with documented venous stasis, a venous insufficiency and ulceration (VLU) greater than 30 days duration, measuring 4 cm<sup>2</sup> to 50 cm<sup>2</sup>, and demonstrated arterial flow were enrolled. Index ulcers were 56 % recurrent, with a median duration of 10.3 months and median ulcer area of 11.0 cm<sup>2</sup>. All participants received protocol-defined SC compression (30 to 40 mm Hg), dressings to promote a moist wound environment, and sharp debridement for a minimum of 1 time per week. Ulcer measurements were obtained weekly using digital planimetry. Pain and QOL scores were assessed at baseline and after 4 weeks of treatment using the visual analog scale and the Short Form-36 Health Survey. After 4 weeks of treatment, the average wound size reduction was 61.6 %  $\pm$  28.9 in the NLFU+SC compared to 45 %  $\pm$  32.5 in the SC group. Reductions in median and absolute wound area as well as pain scores were also significant. The authors concluded that NLFU therapy with guideline-defined standard VLU care should be considered for healing VLUs not responding to SC alone. They stated that the results of this study warrant further research on barriers to healing and the changes occurring in the tissue of the wound. This was not a blinded study.

A randomized, controlled clinical study was conducted by Olyais et al. (2013) to compare the effectiveness of standard treatment and standard treatment plus either high frequency or noncontact low frequency ultrasound when treating chronic wounds, including venous leg ulcers. It was noted that a total of 90 people participated in the study, including 47 men and 43 women. It was also noted that the average age for the participants was 38.3 year old. Out of the 90 participants it was noted that 30 participants received standard care. Standard care was defined as follows: multilayered compression bandaging (40 mm Hg of pressure at the ankle graduated to 17 mm Hg to 20 mm Hg below

the knee), nonadherent dressing, and regular debridement. Standard care dressing changes and ultrasound therapy were provided three times per week for 3 months or until healed. It was noted that 30 participants received standard treatment plus high-frequency ultrasound, which was delivered at 1-3 MHz for 5 to 10 minutes. The remaining 30 participants received standard treatment plus low-frequency ultrasound, which was delivered at 40 kHz for 4-10 minutes. The final results of this study were reported to show that the outcome of both methods of the ultrasound therapy was better than standard care alone. The result of this one study does not provide sufficient clinical data, to change the current unproven status of the use of low frequency ultrasound for the treatment of wounds. Additional studies and randomized trials are required to support and confirm the long and short term findings of this lone study.

Yoa et al. (2012) conducted a randomized clinical study designed to determine the effects of non-contact low frequency ultrasound (NCLF-US) devices when used for the treatment of chronic non healing wounds. Subjects were randomly assigned to one of three groups: application of NCLF-US thrice per week (Group 1), NCLF-US once per week (Group 2) and the control (Group 3) that received no NCLF-US. All subjects received standard wound care plus offloading for a total of 4 weeks. Percent area reduction (PAR) of each wound compared to baseline was evaluated weekly. Twelve DFU patients, 2 (16.7%) type 1 and 10 (83.3%) type 2 diabetics, with an average age of  $58 \pm 10$  years and a total of 12 foot ulcers were enrolled. Group 1 showed significant wound area reduction at weeks 3, 4 and 5 compared to baseline, with the greatest PAR, 86% ( $P < 0.05$ ); Groups 2 and 3 showed 25% PAR and 39% PAR, respectively, but there were no statistically significant differences between Group 2 and Group 3 over time. Based on the information provided by this small randomized study demonstrated that NCLF-US is an effective in treating neuropathic diabetic foot ulcers through at least in part, inhibiting pro-inflammatory cytokines in chronic wound and improving tissue regeneration. Therapeutic application of NFLU three times per week allows for the best wound area reduction. The results of this study must be confirmed in a larger trial.

Ennis et al. (2005) conducted a multicenter, double-blinded randomized controlled trial to evaluate the Mist Therapy<sup>®</sup> System for treatment of chronic diabetic foot ulcers. As an adjunct to standard wound care with saline moistened gauze dressings and debridement as needed, patients underwent true or sham Mist treatment in 3 sessions per week for 12 weeks. Although 133 patients were enrolled and considered in the intent-to-treat analysis, 78 patients (59%) were subsequently excluded leaving 27 patients in the treatment group and 28 in the sham group, which comprised the per protocol population. In the per protocol population, at week 11, the treatment group had a 56% decrease in wound exudation compared with the sham group. In the per protocol population, complete closure was achieved in 41% of patients in the treatment group versus 14% in the sham group at 12 weeks. The mean time to healing was  $9.1 \pm 0.6$  weeks for the treatment group versus  $11.7 \pm 0.2$  weeks for the sham group. Despite the improvements in wound exudation and wound closure for the treatment group versus the sham group, Mist Therapy<sup>®</sup> was not associated with any statistically significant improvements in granulation tissue. According to the intent-to-treat analysis, the Mist Therapy<sup>®</sup> System wound healing did not provide any statistically significant improvements in wound healing.

Watson et al. (2011) assessed the clinical effectiveness of weekly delivery of low dose, high frequency therapeutic ultrasound in conjunction with standard care for hard to heal venous leg ulcers in a multicenter, two arm randomized controlled trial. The study included 337 patients with at least one venous leg ulcer of >6 months' duration or >5 cm (2) area and an ankle brachial pressure index of  $\geq 0.8$ . The study evaluated weekly administration of low dose, high frequency ultrasound therapy for up to 12 weeks plus standard care compared with standard care alone. The two groups showed no significant difference in the time to healing of the reference leg ulcer. After adjustment for baseline ulcer area, baseline ulcer duration, use of compression bandaging, and study center, there was still no evidence of a difference in time to healing. There was no difference in time to complete healing of all ulcers, with median time to healing of 328 days with standard care and 365 days with ultrasound. There was no evidence of a difference in rates of recurrence of healed ulcers (17/31 with ultrasound vs 14/31 with standard care). There was also no difference between the two groups in health related quality of life; both for the physical component score and the mental component score, but there were significantly more adverse events in the ultrasound group. The authors concluded that low dose, high frequency ultrasound administered weekly for 12 weeks during dressing changes in addition to standard care did not increase ulcer healing rates, affect quality of life, or reduce ulcer recurrence.

In a randomized controlled trial, Taradaj et al. (2008) estimated the usefulness of therapeutic ultrasound for healing of venous leg ulcers in 81 patients. Patients in groups 1 and 2 were treated surgically. Patients in groups 3 and 4 were treated conservatively. Patients in groups 1 and 3 were additionally treated with the ultrasound (1 MHz, 0.5 W/cm (2)) once daily, six times a week for seven weeks. Comparison of the number of complete healed wounds indicated statistically significant differences between groups 1 and 4, 2 and 4, 3 and 4 in favor of groups 1, 2 and 3. Comparison of the other parameters also demonstrated more efficient therapy effects in groups 1, 2 and 3 than in group 4. There were no statistical differences in all examined parameters between groups 1, 2 and 3. The investigators concluded that ultrasound is an efficient and useful method only in conservatively treated venous leg ulcers. They state also that there are no special reasons for application of the ultrasound in surgically treated patients. They comment further that a well-conducted surgical operation is much more effective for a healing process than conservative pharmacological procedures. The small study population limits the validity of this study.

Driver et al. (2011) performed a meta-analysis and summarized the effects of a noncontact low-frequency ultrasound (NLFU) therapy on healing of chronic wounds. The meta-analysis included 8 published studies that reported effects of NLFU on wound size and healing rate of chronic wounds in 444 patients. Mean time to healing was 8.2 weeks, with 42% of wounds healed by 12 weeks. The wound volume was reduced by 79.7% over a mean of 12 weeks. According to the authors, noncontact low-frequency ultrasound for treatment of chronic wounds was associated with consistent and substantial wound size reductions, as well as favorable rates of healing. However, the quality of the evidence was limited by small patient numbers and lack of appropriate comparison groups.

Voight et al. (2011) conducted a systematic review and meta-analysis to examine low-frequency (20-30 kHz) ultrasound delivered at either low or high intensity. The objective of the review was to determine whether low-frequency ultrasound used as an adjunctive therapy improves the outcomes of complete healing and reduction of size of chronic lower limb wounds. Eight randomized controlled trials were identified. Three of these trials were unpublished papers presented at conferences. Results demonstrated that early healing (at  $\leq 5$  months) in patients with venous stasis and diabetic foot ulcers was favorably influenced by both high and low-intensity ultrasound delivered at a low frequency-either via contact or noncontact techniques. However, according to the authors, the quality of the evidence is in general of lower quality for both types of ultrasound, and especially for low-frequency low-intensity noncontact ultrasound because of significant biases. The authors stated that although it appears from the meta-analysis performed that low-frequency low-intensity noncontact ultrasound is more effective at complete healing than standard of care, the quality of the evidence as it relates to biases was poor. The study by Ennis et al. (2005) had a significant protocol violation that resulted in 42 patients being dropped from the study. This protocol violation was a result of an inversion of the treatment distances of the treatment protocol between active and sham devices. According to the authors, although there appears to be some clinical benefit with the use of low frequency ultrasound, more and larger size randomized controlled trials should be completed on the longer term clinical effects (i.e.,  $>3$  months) for this therapy.

Cullum et al. (2010) assessed whether ultrasound (US) increases the healing of venous leg ulcers by searching several databases for randomized controlled trials (RCTs) comparing US with no US. Two authors independently assessed the search results and selected eligible studies. Details from included studies were summarized using a data extraction sheet, and double-checked. Eight trials were included; all had unclear, or high, risks of bias, with differences in duration of follow-up, and US regimens. Six trials evaluated high frequency US and five of these reported healing at 7 - 8 weeks. Significantly more patients healed with US than without it at 7 - 8 weeks, but later assessments at 12 weeks showed the increased risk of healing with US was no longer statistically significant. One poor-quality study of high-frequency US found no evidence of an effect on healing after three weeks' treatment. Two trials evaluated low frequency US and reported healing at different time points. Both trials reported no evidence of a difference in the proportion of ulcers healed with US compared with no US: both were significantly underpowered. The authors concluded that the trials evaluating US for venous leg ulcers are small, poor-quality and heterogeneous. They state that there is no reliable evidence that US hastens healing of venous ulcers. There is a small amount of weak evidence of increased healing with US, but this requires confirmation in larger, high-quality RCTs. They conclude that there is no evidence of a benefit associated with low frequency US.

Al-Kurdi et al. (2008) reviewed results from 8 small trials (average enrollment 44 patients) with comparator treatments of either sham ultrasound or standard of care. Studies had either a medium or high risk of bias, which indicates a reduction in study validity. Typical study limitations included lack of allocation concealment and failure to report baseline characteristics, randomization methods, and blinding of outcome assessors. The authors concluded that the available evidence suggests that there may be a benefit from ultrasound therapy in healing venous leg ulcers, however due to the poor quality of the studies; these results need to be interpreted with caution.

In a National Institute for Health and Clinical Excellence (NICE) guidance for MIST Therapy<sup>®</sup> System for the Promotion of Wound Healing in Chronic and Acute Wounds, NICE states that the MIST Therapy<sup>®</sup> System shows potential to enhance the healing of chronic, hard-to-heal, complex wounds, compared with standard methods of wound management. However, the amount and quality of published evidence on the relative effectiveness of the MIST Therapy<sup>®</sup> System is not sufficient, at this time, to support the case for routine adoption of the MIST Therapy<sup>®</sup> System (NICE, 2011, Reaffirmed June 2016).

## **Professional Societies**

### ***Association for the Advancement of Wound Care (AAWC)***

The AAWC released a guideline on the care of pressure ulcers. While noncontact ultrasound therapy was included as a potential second-line treatment if first-line treatments failed to induce wound healing, the strength of the evidence supporting this decision was low (Level C), indicating that there is limited evidence for this technology (AAWC, 2010a).

In a 2010 guideline for venous ulcers, the AAWC states that more evidence is needed to evaluate the use of low frequency ultrasound for venous ulcers (AAWC, 2010b).

### **American College of Foot and Ankle Surgeons**

The American College of Foot and Ankle Surgeons guideline for Diabetic Foot Disorders states that several new ultrasound devices are being used to debride the wound and provide ultrasonic therapy. The guideline also indicates that low-intensity pulsed ultrasound (LIPUS) has also been suggested as a useful adjunct in promoting healing of Charcot fractures. The guideline states that although promising in theory, none of these adjunctive treatments have yet been conclusively proven effective through large prospective multicenter, randomized trials (Frykberg, 2006).

### **National Institute for Health and Care Excellence (NICE)**

The NICE guideline for diabetic foot problems prevention and management recommends one or more of the following as standard care for treating diabetic foot ulcers: offloading; control of foot infection; control of ischemia; wound debridement; and wound dressings. NICE recommends that negative pressure wound therapy should be considered after surgical debridement for diabetic foot ulcers, on the advice of the multidisciplinary foot care service. Dermal or skin substitutes as an adjunct to standard care can be considered when treating diabetic foot ulcers, only when healing has not progressed, and on the advice of the multidisciplinary foot care service (NICE 2016).

### **American Podiatric Medical Association**

The American Podiatric Medical Association in collaboration with the Society for Vascular Surgery and the Society for Vascular Medicine developed a 2016 clinical practice guideline for the management of diabetic foot. Their recommendations do not include warming therapy, noncontact normothermic wound therapy or low frequency ultrasound for the treatment of wounds (Hingorani et al. 2016).

## **U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Warm-Up<sup>®</sup> Active Wound Therapy (Augustine Medical, Inc.) received 510(k) approval from the FDA on March 28, 1997 as a wound and burn occlusive heated dressing. See the following website for more information (use product code MSA): <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed July 11, 2018)

The Mist Therapy<sup>®</sup> System is regulated by the FDA as a Class II device and is classified as an ultrasound wound cleaner. This device was approved via the FDA 510(k) process in April 2004. In May 2005, FDA granted marketing clearance to Celleration for the MIST Therapy<sup>®</sup> System 5.1 with an expanded indication. The approved indication for use is to produce "a low-energy ultrasound-generated mist to promote wound healing through wound cleansing and maintenance debridement by the removal of yellow slough, fibrin, tissue exudates, and bacteria". In 2014 the FDA approved the UltraMIST<sup>®</sup> System (K140782), a smaller, sleeker and user-friendly design. See the following website for more information: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf5/K050129.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf5/K050129.pdf). (Accessed July 11, 2018)

See the following website for additional devices (use product code NRB):  
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>.

In November 2005, the FDA issued a document that outlines the controls applicable to all low-frequency ultrasound devices: Class II Special Controls Guidance Document: Low Energy Ultrasound Wound Cleaner. This document provides nonbinding recommendations to address risks associated with these devices (i.e., delayed wound healing, inflammation, thermal damage, infection, electrical shock) and assure the devices' safety and effectiveness. See the following website for more information:  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071551.htm>.  
(Accessed July 11, 2018)

## **CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)**

Medicare does not cover noncontact normothermic wound therapy as there is insufficient scientific or clinical evidence to consider this device as reasonable and necessary. Refer to the National Coverage Determination (NCD) for [Noncontact Normothermic Wound Therapy \(NNWT\) \(270.2\)](#). Local Coverage Determinations (LCDs) do not exist at this time.

Medicare does not have an NCD for use of low frequency ultrasound in the treatment of wounds. LCDs exist; see the LCDs for [Wound Care](#).  
(Accessed July 19, 2018)

## **REFERENCES**

Alkahtani S, Kunwar P S, Jalilifar M, et al. Ultrasound-based techniques as alternative treatments for chronic wounds: A comprehensive review of clinical applications. *Cureus*. December 2017;9(12): e1952.

Al-Kurdi D, Bell-Syer SE, Flemming K. Therapeutic ultrasound for venous leg ulcers. *Cochrane Database Syst Rev*. 2008 Jan 23;(1):CD001180.

Alvarez OM, Rogers RS, Booker JG, et al. Effect of noncontact normothermic wound therapy on the healing of neuropathic (diabetic) foot ulcers: an interim analysis of 20 patients. *J Foot Ankle Surg*. 2003;42(1):30-35.

Association for the Advancement of Wound Care (AAWC). Pressure Ulcer Guideline. October 2010a. Association for the Advancement of Wound Care (AAWC). Venous Ulcer Guideline. December 2010b.

Chang YR, Perry J, Cross K. Low-frequency ultrasound debridement in chronic wound healing: A systematic review of current evidence. *Plast Surg (Oakv)*. 2017;25(1):21-26.

Cullum NA, Al-Kurdi D, Bell-Syer SE. Therapeutic ultrasound for venous leg ulcers. *Cochrane Database Syst Rev*. 2010 Jun 16;6:CD001180.

Cullum N and Liu Z. Therapeutic ultrasound for venous leg ulcers. *Cochrane Database of Systematic Reviews* 2017. Issue 5. Art. No.: CD001180.

Driver VR, Yao M, Miller CJ. Noncontact low-frequency ultrasound therapy in the treatment of chronic wounds: a meta-analysis. *Wound Repair Regen*. 2011;19(4):475-480.

ECRI Institute. Health Technology Assessment. Mist Therapy System (Alliqua Biomedical, Inc.) Noncontact, Low-frequency Ultrasound for Healing Chronic Wounds. December 2016. Archived report.

Ellis SL, Finn P, Noone M, et al. Eradication of methicillin-resistant *Staphylococcus aureus* from pressure sores using warming therapy. *Surg Infect (Larchmt)*. 2003 Spring;4(1):53-5.

Ennis WJ, Foremann P, Mozen N, et al. Ultrasound therapy for recalcitrant diabetic foot ulcers: results of a randomized, double-blind, controlled, multicenter study. *Ostomy Wound Manage*. 2005;51(8):24-39. Erratum in: *Ostomy Wound Manage*. 2005;51(9):14.

Frykberg RG, Zgonis T, Armstrong DG, et al. American College of Foot and Ankle Surgeons. Diabetic foot disorders: a clinical practice guideline. *J Foot Ankle Surg* 2006 Sep-Oct;45(5):S2-66.

Gibbons GW, Orgill DP, Serena TE, et al. A prospective, randomized, controlled trial comparing the effects of noncontact, low-frequency ultrasound to standard care in healing venous leg ulcers. *Ostomy Wound Manage*. 2015;61(1):16-29.

Hayes, Inc. Hayes Medical Technology Directory Report. Noncontact Low-Frequency Ultrasound Using the MIST Therapy System (Celleration Inc.) for Treatment of Lower Extremity Arterial and Diabetic Foot Ulcers. Lansdale, PA: Hayes. June 30, 2016a. Updated June 8, 2018.

Hayes, Inc. Hayes Medical Technology Directory Report. Noncontact Low-Frequency Ultrasound Using the MIST Therapy System (Celleration Inc.) for Treatment of Venous Leg Ulcers. Lansdale, PA: Hayes. June 30, 2016b. Updated June 8, 2018.

Hingorani Anil, LaMuraglia Glenn, Henke Peter, 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. *Journal of Vascular Surgery*. February 2016;63(25).

Karr JC. External thermoregulation of wounds associated with lower-extremity osteomyelitis: A pilot study. *J Am Podiatr Med Assoc*. 2003;93(1):18-22.

Kavros SJ, Miller JL, Hanna SW. Treatment of ischemic wounds with noncontact, low-frequency ultrasound: The Mayo Clinic Experience, 2004-2006. *Adv Skin Wound Care*. 2007;20(4):221-226.

Kloth LC, Berman JE, Nett M, et al. A randomized controlled clinical trial to evaluate the effects of noncontact normothermic wound therapy on chronic full-thickness pressure ulcers. *Adv Skin Wound Care*. 2002;15(6):270-276.

McCulloch J, Knight CA. Noncontact normothermic wound therapy and offloading in the treatment of neuropathic foot ulcers in patients with diabetes. *Ostomy Wound Manage*. 2002;48(3):38-44.

Murphy CA, Houghton P, Brandys T, et al. The effect of 22.5 kHz low-frequency contact ultrasound debridement (LFCUD) on lower extremity wound healing for a vascular surgery population: A randomized controlled trial. *Int Wound J*. 2018 Jun;15(3):460-472.

National Institute for Health and Care Excellence (NICE). The MIST Therapy system for the promotion of wound healing. London, UK: NICE. July 2011. Reaffirmed June 2016.

National Institute for Health and Care Excellence (NICE). NG19. Diabetic foot problems: prevention and management. January 2016.

Olyaei M, Rad FS, Elahifar MA, et al. High-frequency and noncontact low frequency ultrasound therapy for venous leg ulcer treatment: a randomized, controlled study. *Ostomy Wound Manage*. 2013 Aug;59(8):14-20.



Taradaj J, Franek A, Brzezinska-Wcislo L, et al. The use of therapeutic ultrasound in venous leg ulcers: a randomized, controlled clinical trial. *Phlebology*. 2008;23(4):178-83.

Thomas DR, Diebold MR, Eggemeyer LM. A controlled, randomized, comparative study of a radiant heat bandage on the healing of stage 3-4 pressure ulcers: a pilot study. *J Am Med Dir Assoc*. 2005 Jan-Feb;6(1):46-9.

Tricco AC, Antony J, Vafaei A, et al. Seeking effective interventions to treat complex wounds: An overview of systematic reviews. *BMC Med*. 2015;13:89.

Voigt J, Wendelken M, Driver V et al. Low-frequency ultrasound (20-40 kHz) as an adjunctive therapy for chronic wound healing: A systematic review of the literature and meta-analysis of eight randomized controlled trials. *Int J Low Extrem Wounds*. 2011;10(4):190-199.

Watson JM, Kang'ombe AR, Soares MO, et al; VenUS III Team. Use of weekly, low dose, high frequency ultrasound for hard to heal venous leg ulcers: the VenUS III randomized controlled trial. *BMJ*. 2011 Mar 8;342:d1092.

White J, Ivins N, Wilkes A, et al. Non-contact low-frequency ultrasound therapy compared with UK standard of care for venous leg ulcers: A single-centre, assessor-blinded, randomised controlled trial. *Int Wound J*. 2015 Jan 25.

Whitney JD, Salvadalena G, Higa L, et al. Treatment of pressure ulcers with noncontact normothermic wound therapy: healing and warming effects. *J WOCN*. 2001;28(5):244-252.

Yao M, Hasturk H, Kantarci A, Gu G, et al. A pilot study evaluating noncontact low frequency ultrasound and underlying molecular mechanism on diabetic foot ulcers. *Int Wound J*. 2012 Nov 19.

Yue J, Zhang S, Sun Q, et al. Local warming therapy for treating chronic wounds: A systematic review. *Medicine* (2018) 97:12.

#### POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
12/01/2018	<ul style="list-style-type: none"><li>Simplified coverage rationale (no change to guidelines)</li><li>Archived previous policy version 2018TO521M</li></ul>

#### INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.