

Topical Oxygen Therapy

Policy Number: SRST2026T0632K

Effective Date: October 1, 2026

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Related Policies

None

Coverage Rationale

Topical Oxygen Therapy is unproven and not medically necessary for the treatment of wounds or ulcers due to insufficient evidence of efficacy.

Definitions

Topical Oxygen Therapy: The direct application of oxygen to a wound site. Topical Oxygen Therapy can be applied intermittently to an open wound at slightly above atmospheric pressure or applied continuously through a cannula secured under a wound dressing covered by film. (ECRI, 2019; updated 2025)

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 guidelines may apply.

HCPSC Code	Description
A4575	Topical hyperbaric oxygen chamber, disposable
E0446	Topical oxygen delivery system, not otherwise specified, includes all supplies and accessories

Description of Services

Topical Oxygen Therapy delivers oxygen directly to the wound surface to improve oxygenation in hypoxic tissue, particularly when local blood flow is inadequate. Using commercially available systems, oxygen is applied at slightly above atmospheric pressure within a sealed enclosure placed over the wound or affected limb. Treatment may consist of 90-minute sessions administered three to five times per week or continuous therapy. All wound dressings must be removed during application to allow effective transcutaneous oxygen delivery. Another approach uses a Topical Oxygen Therapy device that delivers continuous oxygen through a cannula positioned beneath a wound dressing and secured with an occlusive film. (ECRI, 2019; updated 2025)

Topical Oxygen Therapy

Quality evidence in peer-reviewed, medical literature that evaluated topical oxygen therapy (TOT) is limited. Future robust RCTs are warranted, along with long-term outcomes, to establish the safety and efficacy of this treatment.

Zhu et al. (2026) conducted a two-arm RCT evaluating the efficacy and safety of a portable continuous diffusion of oxygen (CDO) TOT system vs. those of moist wound therapy in adults with chronic wounds. The study enrolled participants aged ≥ 18 years who had wounds persisting for > 4 weeks and measuring 2 to 25 cm² and ≥ 0.5 cm deep; could adhere to treatment; and had no dressing sensitivities. The exclusion criteria included secondary osteomyelitis or malignant wounds; active bleeding; wounds in locations difficult to seal; severe systemic illness impairing healing; use of immunosuppressive, steroidal, or chemotherapeutic agents; or participation in another clinical trial within the past 3 months. The study's primary outcomes were the percentage reduction in wound area at day 28 and the wound healing rate at both day 28 and week 12. Overall, 88 participants were randomized to receive either TOT ($n = 44$) or moist wound therapy ($n = 44$) for a 28-day treatment period, with any unhealed wounds subsequently managed using standardized moist wound therapy through week 12. Weekly assessments measured wound area, depth, pH, healing rate, healing time, and adverse events. By day 28, TOT produced significantly greater reductions in wound area and depth and resulted in lower wound bed pH than moist wound therapy. The TOT group had a substantially higher healing rate at day 28 (45.5% vs. 11.4%), but by week 12, both groups reached similarly high healing rates (95.5% vs. 90.9%; $p = 0.536$). The overall healing time was shorter with TOT by an average of 13.5 days, and no TOT-related adverse events were observed. The authors concluded that portable TOT markedly accelerates healing in chronic wounds, with reductions in wound bed pH contributing to improved conditions that promote subsequent tissue repair processes. The study's limitations include its single-center design and modest sample size; heterogeneity of wound types and comorbidities that prevented subgroup analyses, especially for DFUs and venous leg ulcers; and a short 12-week follow-up period that limited assessment of long-term healing and recurrence.

A 2025 Hayes Evolving Evidence Review indicated that continuous TOT appears reasonably safe as an adjunctive treatment for DFUs, with most reported adverse events being mild to moderate and only a small proportion considered possibly or probably related to the device. The addition of continuous TOT to conventional wound therapy was not associated with an increased risk of adverse events. Evidence from full-text clinical studies and systematic reviews provides moderate support for continuous TOT as an adjunct to standard care in the management of chronic DFUs, although clinical practice guidelines and professional position statements offer only weak endorsement. Overall, while safety data are reassuring and the existing evidence suggests potential benefit, stronger and more consistent guideline support will likely require additional high-quality studies.

OuYang et al. (2024) conducted a network meta-analysis comparing various treatment strategies for DFUs and assessing their effects on ulcer healing. The analysis included 57 RCTs, involving 4,826 individuals. The study found that TOT improved complete ulcer healing rates compared with standard of care in both direct and network meta-analyses. However, TOT did not show a measurable advantage over other treatments in reducing ulcer area or shortening healing time, which were benefits that were primarily associated with platelet-rich plasma and negative pressure wound therapy. In terms of safety outcomes, including amputation rates and adverse events, TOT did not differ significantly from other interventions. Although TOT outperformed the standard of care, it did not rank among the most effective treatments in the network analysis, in which combination therapies involving platelet-rich plasma and negative pressure wound therapy demonstrated the highest overall performance across healing, size reduction, healing time, and safety outcomes. According to the authors, DFU treatment often works best when multiple therapies are combined. Clinicians can tailor single or combined treatments, based on the ulcer's characteristics, and weigh the benefits and risks for each individual. The authors suggested that more clinical trials are needed to further evaluate the effectiveness of combination therapies for DFUs. The study's limitations include variability in individuals' demographics, inconsistent measurement timing across studies, and lack of blinding.

Putri et al. (2024) conducted a systematic review and meta-analysis that evaluated seven RCTs ($n = 692$) and two observational studies ($n = 111$) that compared supplemental TOT with standard wound care. The rate of healed wounds was 25.8% in the control group and 43.25% in the adjuvant TOT group, which showed that the use of TOT significantly increased the number of healed wounds (RR, 1.77; 95% CI, 1.18-2.64; $p = 0.005$). A significant decrease in the percentage of wound area was found in the TOT group in RCT studies (mean difference, 15.64; 95% CI, 5.22-26.06; $p = 0.003$). In observational studies, the rate of healed wounds was 37.5% in the standard care group and 80.95% in the adjuvant TOT group, which showed a significant increase in the number of healed wounds in the adjuvant TOT group (RR, 2.15; 95% CI, 1.46-3.15; $p < 0.00001$). The authors concluded that TOT is an effective adjunctive treatment for chronic wound healing, especially for wounds with vascular compromise, such as diabetic ulcers and pressure ulcers.

However, the authors noted that further research is needed to explore the potential applications of this technology across various types of wounds and for TOT as a main or sole treatment. Limitations include the short follow-up periods and small sample sizes in some of the studies. Tawfick and Sultan (2009) and Blackman et al. (2010), previously cited in this policy, are included in this review. He et al. (2021) is also included in this review.

Carter et al. (2023) conducted a systematic review and meta-analysis of four RCTs that compared adjunctive TOT with a control group of individuals receiving standard-of-care treatments (debridement, off-loading, and moist wound care) for Wagner 1 and 2 DFUs. The primary outcome of interest was complete wound healing at 12 weeks, and the secondary outcomes were wound-related pain, hospital readmissions, QOL, adverse effects, dependence on or need for outside care, and adherence to the prescribed therapy. Risk-of-bias judgment (RoB2 analysis) resulted in one low-risk trial and three trials with some risk. One study was determined to be the origin of the statistical heterogeneity. The pooled results showed statistical significance, with an RR of 1.59 (95% CI, 1.07-2.37; $p = 0.021$). A sensitivity analysis, based on imputed values for missing outcomes, demonstrated that both the RR and 95% CIs changed little. The GRADE (Grading of Recommendations Assessment, Development, and Evaluation) ratings for each domain were moderate (3) for risk of bias; moderate (2) and high (1) for imprecision; low (2) and high (1) for inconsistency; moderate (2) and high (1) for indirectness; and moderate (1) and high (2) for publication bias. Overall, the evidence was noted as moderate. The authors concluded that in the absence of infection and ischemia, TOT was a viable treatment for Wagner 1 and 2 DFUs. Limitations include the short-term follow-up and small study size; additionally, the confidence in the authors' conclusions may be limited by their stated financial conflicts of interest.

Sun et al. conducted a 2022 systematic review and meta-analysis evaluating the efficacy and safety of TOT for DFUs, ultimately including seven studies that involved 614 individuals. Eligible studies were those that enrolled individuals with DFUs who were using TOT either alone or alongside standard care, comparing with standard care controls and reporting outcomes such as ulcer healing, ulcer area, healing time, adverse events, follow-up, or QOL measures; studies that lacked essential data, abstracts only, duplicate interim reports, and trial protocols were excluded. The included studies, most involving continuous diffusion oxygen therapy and others evaluating intermittent TOT, consistently showed that TOT improved healing outcomes, with a higher healing rate (RR, 1.63; 95% CI, 1.33-2.00) and qualitative evidence of reduced ulcer area, greater healing durability, and enhanced QOL, without an increase in adverse events; however, its effect on healing time remained uncertain. The authors concluded that existing evidence supports TOT as an effective and safe option for DFUs, although further high-quality research is needed to clarify mechanisms and optimize treatment strategies. Limitations include inconsistent eligibility criteria, variable interventions and treatment durations, heterogeneity in care delivery settings, insufficient data for comparing continuous vs intermittent TOT, and a lack of additional double-blinded, placebo-controlled trials.

He et al. (2021) conducted a single-center RCT to determine the effect of CDO combined with traditional moist wound dressing (MWD) on the DFUs of inpatients. Participants were randomly divided into three groups that consisted of 40 participants each. One group received the moist dressing, one group was treated with a micro-oxygen supply device, and one group received a combination of moist dressing and a micro-oxygen supply device. The amputation rate, wound healing, and inflammatory control were evaluated after 8 weeks of treatment. Compared with the MWD and CDO groups, the combination group had a higher wound healing rate ($p < 0.05$), lower white blood cell count ($p < 0.05$), and lower high-sensitivity C-reactive protein level ($p < 0.05$). During the 1-year follow-up, the amputation rate was 0% in the combination group, which was significantly lower than that in the other two groups ($p < 0.05$). The authors concluded that the combination treatment of MWD and CDO was effective in preventing infection and promoting healing of DFUs. Limitations include a small sample size and lack of molecular mechanism exploration. The authors recommended larger, randomized, double-blinded studies in the future.

An ECRI Evidence Analysis (2019) that evaluated the safety and efficacy of TOT for treating DFUs compared with those of standard of care, such as debridement, moisture balance maintenance with dressing, and infection control, found that TOT added to the standard of care appeared to increase DFU healing more than the standard of care alone. In the updated 2025 ECRI summary, evidence from three systematic reviews showed that adding TOT to standard care improves DFU healing compared with standard care alone. One network meta-analysis suggested that TOT may be less effective than platelet-rich plasma, stem cells, or platelet-rich plasma combined with negative pressure wound therapy; however, more high-quality, head-to-head studies are needed to confirm this. Additional RCTs are also needed to identify the optimal TOT application method and to directly compare TOT with other therapies.

Clinical Practice Guidelines

International Working Group on the Diabetic Foot (IWGDF)

Chen et al. (2024) developed an IWGDF guideline that states that the use of TOT as an adjunct therapy to standard of care for wound healing in people with diabetes-related foot ulcers, for which standard of care alone has failed and

resources exist to support this intervention, may be considered. Strength of recommendation: conditional; certainty of evidence: low.

National Institute for Health and Care Excellence (NICE)

NICE (2020) performed an innovation briefing that states that the NATROX device delivers 98% humidified oxygen directly and continuously to a wound through a flexible tube from a portable oxygen generator and is used to treat chronic, nonhealing wounds such as DFUs. The briefing included three studies that consisted of one small RCT and two larger observational studies. According to NICE, while the evidence shows that the NATROX device had an effect, the small sample sizes and heterogeneous populations involved reduced the overall significance of the findings.

Undersea and Hyperbaric Medical Society (UHMS)

The UHMS states that application of topical oxygen cannot be recommended in routine clinical treatment due to a restricted volume and quality of supporting scientific evidence. According to the UHMS, before topical oxygen can be recommended as a therapy for nonhealing wounds, its application should be subjected to additional scientific scrutiny to better establish indications for use, response to treatment, and dosing. (UHMS, 2018)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. U.S. Food and Drug Administration (FDA)—approval alone is not a basis for coverage.

Topical oxygen therapy devices are regulated by the FDA as Class II devices, and several devices have been approved via the FDA 510(k) process. Refer to the following website for more information (use product code KPJ): <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed June 22, 2026)

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Policy History/Revision Information

Date	Summary of Changes
10/01/2026	Title Change - Previously titled <i>Hyperbaric Oxygen Therapy and Topical Oxygen Therapy</i> Coverage Rationale - Removed content/language pertaining to hyperbaric oxygen therapy Definitions - Removed definition of: - Hyperbaric Oxygen Therapy - Mild Hyperbaric Oxygen Therapy Applicable Codes - Removed CPT/HCPCS codes 99183 and G0277 - Removed list of applicable ICD-10 diagnosis codes Supporting Information - Updated <i>Description of Services</i>, <i>Clinical Evidence</i>, <i>FDA</i>, and <i>References</i> sections to reflect the most current information - Archived previous policy version 2026T0632J

Instructions for Use

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