Molina Clinical Policy
Topical Oxygen Therapy
Policy No. 050

Last Approval: 04/08/2026
Next Review Due By: April 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Topical oxygen therapy (TOT) is a wound-care approach that delivers oxygen directly to the surface of a skin wound using devices such as diffusion systems, cannulas, or oxygen-permeable dressing. The Undersea & Hyperbaric Medical Society (UHMS) does not classify TOT as a form of hyperbaric oxygen therapy and notes that it does not reproduce the systemic physiological responses associated with hyperbaric treatment (UHMS 2018). Although some recent studies suggest that TOT may support wound healing in selected clinical scenarios, the current body of evidence remains limited, and additional research is needed to clarify its clinical value, ideal treatment parameters, and long-term outcomes.

TOT functions by supplying oxygen directly to the wound bed and the surrounding tissue and can be delivered either intermittently or continuously. Intermittent topical oxygen therapy uses concentrated oxygen, typically around 93 percent, administered for scheduled sessions similar in timing to hyperbaric protocols, often involving 90-minute treatments several times per week. These systems typically operate at pressures slightly above normal atmospheric levels and use a sealed chamber or enclosure around the affected area. Continuous topical oxygen therapy, on the other hand, provides a steady flow of humidified oxygen exceeding 99 percent concentration, generated by a small portable device that allows sustained, low-flow application directly to the wound surface. The actual dose of oxygen reaching the tissue depends on multiple factors, including oxygen concentration, pressure, delivery method, and total duration of exposure. TOT is currently being investigated primarily as a potential option for individuals who are unable to undergo hyperbaric oxygen therapy or who require an additional modality when conventional wound care does not achieve adequate healing (Oropallo & Evans 2026).

Regulatory Status

TOT devices fall under the FDA's Class II medical device category, and many products have obtained 510(k) clearance under product code KPJ (FDA 2025).

COVERAGE POLICY

Topical oxygen therapy is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

SUMMARY OF MEDICAL EVIDENCE

Randomized Controlled Trials

Zhu et al. (2024) reported results of a randomized controlled trial comparing a portable continuous-diffusion topical oxygen therapy (TOT) protocol against standardized moist wound therapy (MWT) for chronic wounds. Adults ≥18 years with chronic wounds persisting >4 weeks, wound area 2–25 cm² and depth ≥0.5 cm, adequate cognition/ability to comply, and no dressing allergies were randomized 1:1 (n=88; 44 per arm) after standardized wound-bed preparation. Patients were excluded for secondary osteomyelitis or malignant wounds, active bleeding, locations not amenable to sealing, severe systemic conditions compromising healing (e.g., uncontrolled diabetes, malnutrition, organ failure), immunosuppressive/chemotherapy or steroid use, or recent trial participation. Primary outcomes were percentage wound-area reduction at day 28 and complete healing rates at day 28 and week 12; secondary outcomes included wound-bed pH, percentage depth reduction, time to complete healing, adverse events, and exploratory subgroup analyses by wound etiology. At day 28, TOT produced greater wound-area reduction than MWT ($p<0.001$) and larger depth reduction ($p=0.018$), with lower wound-bed pH at day 14 and 28 ($p=0.005$; $p=0.007$). Day-28 healing favored TOT ($p<0.001$), and mean time-to-healing was shorter with TOT by ~13.5 days at week 12 ($p=0.004$). By week 12, overall healing rates converged ($p=0.536$). No TOT-related adverse events were observed. Limitations included single-center design, modest sample size, heterogeneity of wound etiologies with relatively few DFU/VLU cases, limited power for multivariable analyses, and 12-week follow-up that does not address long-term durability or recurrence. The study supports portable continuous TOT as a potentially useful early-phase treatment for chronic wounds, but more comprehensive evidence is required before its long-term clinical value can be established.

Al-Jalodi et al. (2022) conducted a multicenter randomized clinical trial with a one-year prospective follow-up to assess the durability of diabetic foot ulcer (DFU) healing among patients previously treated either with topical oxygen therapy combined with standard care or with standard care alone. The long-term cohort consisted of adults who had completed the NOW.T-001 parent trial and met eligibility criteria including being at least 18 years old, having a chronic DFU of 0.5 to 25 cm² that failed to improve adequately after four weeks of standard care, demonstrating sufficient lower-extremity perfusion, and maintaining ISDA grade 1 or 2 disease while meeting all protocol and consent requirements. Patients were excluded if they had limited life expectancy, significant comorbid disease that could interfere with therapy, wound characteristics preventing oxygen exposure, recent use of biologics or immunosuppressive medications, active malignancy in the wound region, uncontrolled diabetes, need for hyperbaric oxygen therapy, or evidence of substantial spontaneous healing during the preparatory period. The primary goal of the long-term study was to determine whether ulcers that had closed by 12 weeks remained healed over the subsequent 12 months, with recurrence defined as reopening in the same location and secondary outcomes capturing new ulcers or major clinical events. Of the 54 participants who achieved closure in the original trial, 29 agreed to one-year monitoring; the data showed that 85 percent of ulcers in the topical-oxygen group remained closed at one year compared with 60 percent in the standard-care group, with fewer recurrences and one major amputation occurring only in the standard-care arm. The study was limited by the modest sample size, reduced follow-up participation, and disruptions caused by the COVID-19 pandemic, all of which constrained statistical analysis. The observed pattern of more persistent ulcer closure in the topical-oxygen cohort suggests a potential long-term advantage and supports the need for larger, more definitive trials to clarify the role of topical oxygen therapy in sustaining DFU healing.

Frykberg et al. (2020) completed a prospective, multinational, multicenter, randomized, double-blinded, placebo-controlled randomized clinical trial to assess the efficacy of multimodality cyclical pressure Topical Wound Oxygen (TWO2) home care therapy in healing refractory diabetic foot ulcers that had failed to heal with standard of care alone. A total of 220 patients were enrolled in the study with 110 randomized on a 1:1 basis to either sham or active TWO2 therapy. Both treatment arms received sham or TWO2 therapy in addition to standard of care. The primary outcome measured was the percentage of ulcers achieving 100% healing at 12 weeks and secondary outcomes included ulcer recurrence, incidence of amputation, and quality of life index. Results were reported on the first 73 participants enrolled in the study (sham = 36, active TWO2 = 37) and showed that “the active TWO2 arm showed > 3.5 times the likelihood to completely heal over 12 weeks compared with the sham arm” (HR 3.64, 97.8% CI, p = 0.013). Ulcer recurrence was assessed at 12 months post-enrollment, with only one recurrence out of 15 healed ulcers in the active TWO2 arm and two recurrences out of five healed ulcers in the sham arm. Of note, 20 ulcers were reported as closed at 12 months in the active TWO2 arm compared to 10 in the sham arm. Overall quality of life indexes improved in both treatment arms with greater increases noted in the active TWO2 arm. Therapy compliance and off-loading device compliance was

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

high in each treatment arm. A total of 10 serious adverse events and eight adverse events occurred in each treatment arm with two index limb amputations occurring in the active TWO2 arm compared to three index limb amputations in the sham arm. Researchers noted a major limitation of this study was the small sample size due to predetermined "hard stopping rules" that limited analysis to the first 73 patients enrolled due to a significant number of patients in the active TWO2 arm healing compared to those in the sham arm. Researchers concluded that the results of this study are promising, but additional studies are needed to determine efficacy as the current published evidence has several methodological weaknesses.

Systematic Reviews and Meta-Analyses

Putri et al. (2024) conducted a meta-analysis of randomized controlled trials and controlled observational studies to assess the efficacy of topical oxygen therapy (TOT) for wound healing. Studies included trials that compared adjuvant TOT against standard wound care in adults with chronic wounds and reported heal/closure and related endpoints, while excluding nonrandomized or uncontrolled designs for the RCT pool, studies without extractable outcomes, or duplicates. Across seven RCTs (n=692) and two controlled observational studies (n=111), adjuvant TOT increased the proportion of completely healed wounds versus control in RCTs (p=0.005), reduced wound area (p=0.003), and, in observational cohorts, was associated with higher healing rates (p<0.00001). The authors noted heterogeneity across studies, device and dosing variability, and the inclusion of observational data, all of which temper certainty and limit generalizability. The analysis supports TOT as a potentially beneficial adjunct to standard care for chronic wounds, improving the likelihood of short-term closure and wound size reduction, but larger, methodologically rigorous RCTs with standardized protocols are needed to confirm durable benefit and define optimal candidates and regimens.

Sun et al. (2022) completed a meta-analysis and systematic review to evaluate the safety and efficacy of topical oxygen therapy as a treatment for diabetic foot ulcers. A total of 7 studies with 614 participants were included in the meta-analysis. Five studies used continuous diffusion of oxygen therapy and two studies used intermittent topical oxygen therapy. Wounds were assessed using the Texas grading system in four studies and the Wagner grading system in three studies. There was a relatively high risk of bias among all the studies with two studies being funded by device manufacturers, two studies having a high risk of selective reporting due to inadequacies in the reporting of adverse events, and one study having a high risk of attrition bias. Outcomes reported included the number of ulcers that completely healed, mean ulcer area, healing time, follow-up, and quality of life. Pooled results of six studies showed that a higher number of ulcers were completely healed at either eight or 12 weeks in the topical oxygen therapy group (topical oxygen therapy = 148/346, control = 86/330, $p < 0.00001$). Five studies reported the mean ulcer area; however, two of the studies were excluded from meta-analysis due to inconsistencies in intervention durations. Pooled results for mean ulcer area, adverse events, follow-up, and quality of life suggested improved outcomes in the topical oxygen therapy groups. Healing time was reported by four studies with pooled analysis suggesting unclear effects on healing time in the topical oxygen therapy groups. Of note, one study reported significantly improved healing times in the ≥ 65-year-old subgroup ($p < 0.05$). Researchers noted that the results of this meta-analysis were promising for the use of topical oxygen therapy as an adjunct treatment in diabetic foot ulcers. However, researchers noted more robust and well-controlled trials are needed to confirm the results of existing trials due inconsistencies with predefined outcomes and the severity of ulcers treated with topical oxygen therapy compared to the control groups.

National/Specialty Organizations

The **American Diabetes Association (ADA)** published *Standards of Care in Diabetes* which maintains a high-level recommendation for adjunctive topical oxygen therapy in non-healing diabetic foot ulcers after appropriate standard care has been attempted. ADA's grading communicates strong support for short-term benefits in selected DFU populations while recognizing the need for continued research on durability of closure and standardized protocols (ADA 2025).

The **International Working Group on the Diabetic Foot (IWGDF)** conditionally recommends considering topical oxygen as an adjunct to standard of care in people with diabetes-related foot ulcers when standard care alone has failed and resources are available to support the intervention. This stance reflects expanding, including several randomized trials aggregated in the 2023 guideline update on interventions to enhance healing. The recommendation is not a strong endorsement; rather, it signals cautious adoption in selected, non-healing DFU cases while acknowledging ongoing uncertainty about optimal patient selection and treatment parameters (Schaper et al. 2024).

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

The **Undersea & Hyperbaric Medical Society (UHMS)** published the *UHMS Position Statement: Topical Oxygen for Chronic Wounds* which concludes that while topical oxygen may be a promising treatment based on some recent studies, it cannot be recommended for routine clinical use at this time due to a lacking volume and quality of supporting scientific evidence. More investigation is needed to determine if it can be used in the clinical setting for wound care. Before topical oxygen therapy can be recommended for non-healing wounds, its application should be subjected to additional scientific scrutiny to better establish indications for use, dosing, and response to treatment (UHMS 2018).

The **Wound Healing Society (WHS)** elevated topical oxygen therapy to Level 1 evidence in updated guidance for diabetic foot ulcer care and states that topical oxygen has been shown to increase the incidence of healing and decrease time to heal. WHS's upgrade reflects cumulative randomized and systematic evidence, particularly in DFUs, and underscores that TOT may be considered as an advanced adjunctive modality in carefully selected non-healing wounds within a comprehensive wound-care program (Lavery et al. 2024).

CODING & BILLING INFORMATION

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
E0446	Topical oxygen delivery system, not otherwise specified, includes all supplies and accessories

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

04/08/2026	Policy reviewed, no changes to criteria. Updated Overview, Summary of Medical Evidence, and References.
04/09/2025	Policy revised to remove Hyperbaric Oxygen Therapy criteria. Hyperbaric Oxygen Therapy criteria retired in lieu of MCG A-0250. Topical Oxygen Therapy criteria remains E/I/U.
04/10/2024	Policy reviewed, no changes to criteria. Updated Overview, Summary of Medical Evidence, and References. IRO Peer Review on February 21, 2024, by a practicing, board-certified physician with specialties in Undersea & Hyperbaric Medicine and Occupational Medicine.
04/13/2023	Policy reviewed. Coverage criteria updated to include initial authorization of up to 20 sessions with prior authorization being required for additional sessions. Updated Overview, Summary of Medical Evidence, and References.
04/13/2022	Policy reviewed, updated Overview, Summary, References. Updated policy name to include Topical Oxygen Therapy.
04/05/2021	Policy reviewed, no changes to criteria. Updated references.
04/23/2020	Policy reviewed, no changes to criteria.
06/19/2019	Policy reviewed, no changes to criteria.
03/08/2018	Policy reviewed, no changes to criteria.
12/16/2009	MCR no longer scheduled for revision.
04/30/2008	New policy.

REFERENCES

1. Al-Jalodi O, Kupcella M, Breisinger K, et al. A multicenter clinical trial evaluating the durability of diabetic foot ulcer healing in ulcers treated with topical oxygen and standard of care versus standard of care alone 1 year post healing. Int Wound J. 2022 Nov;19(7):1838-1842. doi: 10.1111/iwj.13789. Epub 2022 Apr 19. PMID: 35437881; PMCID: PMC9615268.
2. American Diabetes Association Professional Practice Standards of Care in Diabetes-2025. Diabetes Care. 2025 Jan 1;48(1 Suppl 1):S181-S206. doi: 10.2337/dc25-S009. PMID: 39651989; PMCID: PMC11635045.
3. Frykberg RG, Franks PJ, Edmonds M, et al. A multinational, multicenter, randomized, double-blinded, placebo-controlled trial to evaluate the efficacy of cyclical topical wound oxygen (TWO2) therapy in the treatment of chronic diabetic foot ulcers: The TWO2 study. Diabetes Care. 2020 Mar;43(3):616-624. doi: 10.2337/dc19-0476. Epub 2019 Oct 16. PMID: 31619393.
4. Lavery LA, Suludere MA, Attinger CE, et al. WHS (Wound Healing Society) guidelines update: Diabetic foot ulcer treatment guidelines. Wound Repair Regen. 2024 Jan-Feb;32(1):34-46. doi: 10.1111/wrr.13133. Epub 2023 Dec 21. PMID: 38032324.
5. Oropallo A, Ecans K. Overview of treatment of chronic wounds. Updated Febaury 17, 2026. Accessed March 13, 2026. http://www.uptodate.com.
6. Putri IL, Alyssa A, Aisyah IF, et al. The efficacy of topical oxygen therapy for wound healing: A meta-analysis of randomized controlled trials and

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*

observational studies. Int Wound J. 2024 Jul;21(7):e14960. doi: 10.1111/iwj.14960. PMID: 38984473; PMCID: PMC11234139.
7. Schaper NC, van Netten JJ, Apelqvist J, et al. Practical guidelines on the prevention and management of diabetes-related foot disease (IWGDF 2023 update). Diabetes Metab Res Rev. 2024 Mar;40(3):e3657. doi: 10.1002/dmrr.3657. Epub 2023 May 27. PMID: 37243927.
8. Sun XK, Li R, Yang XL, et al. Efficacy and safety of topical oxygen therapy for diabetic foot ulcers: An updated systematic review and meta-analysis. Int Wound J. 2022 Dec;19(8):2200-2209. doi: 10.1111/iwj.13830. Epub 2022 May 5. PMID: 35510518; PMCID: PMC9705166.
9. Undersea and Hyperbaric Medical Society (UHMS). UHMS position statement: Topical oxygen for chronic wounds. Published 2005. Revised May 23, 2018. Accessed March 13, 2026. https://www.uhms.org/resources/featured-resources/position-statements.html
10. United States Food and Drug Administration (FDA). 510(k) database. Search: Topical Oxygen Therapy. Product Code KPJ. Accessed April 7, 2025. https://www.fda.gov
11. Zhu Y, Jiang Q, Zhan Y, et al. Clinical Efficacy and Safety of Portable Continuous Topical Oxygen Therapy for Chronic Wound Management: A Randomised Controlled Trial. Int Wound J. 2026 Feb;23(2):e70837. doi: 10.1111/iwj.70837. PMID: 41605221; PMCID: PMC12851797.

Molina Healthcare, Inc. ©2026 – *This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare.*