

## 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)**, which includes traditional intermittent application and newer continuous diffusion methods, delivers gaseous oxygen to a cutaneous wound through a cannula, diffusion system, or oxygen-permeable dressing. The UHMS and Centers for Medicare and Medicaid Services (CMS) do not recognize TOT as Hyperbaric Oxygen Therapy because it lacks systemic exposure and fails to provide the same mechanisms of action and physiological effects. While TOT shows promise in some recent studies, further research is needed to establish its safety, efficacy, and appropriate clinical use. Additional scientific scrutiny is necessary to define indications, optimize dosing, and assess treatment response (UHMS 2018; CMS 2023).

### Regulatory Status

TOT devices are regulated Class II medical devices, and many have been cleared through the FDA 510(k) process under product code KPJ.

## 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.

## SUMMARY OF MEDICAL EVIDENCE

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 Clinical Policy

## Topical Oxygen Therapy: Policy No. 050

Last Approval: 04/09/2025  
Next Review Due By: April 2026



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.

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  $\geq 65$ -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 to inconsistencies with predefined outcomes and the severity of ulcers treated with topical oxygen therapy compared to the control groups.

### National/Specialty Organizations

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 **International Working Group on the Diabetic Foot (IWGDF)** published updated guidelines in 2019 on the use of interventions to enhance the healing of chronic diabetic foot ulcers. Topical oxygen therapy is not recommended as a primary or adjunctive treatment (Rayman et al. 2020).

## CODING & BILLING INFORMATION

### HCPSC (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

**04/09/2025** Policy revised to remove Hyperbaric Oxygen Therapy criteria. Hyperbaric Oxygen Therapy criteria retired in lieu of MCG A-0250.

# Molina Clinical Policy

## Topical Oxygen Therapy: Policy No. 050

Last Approval: 04/09/2025

Next Review Due By: April 2026



	Topical Oxygen Therapy criteria remains E//U.
<b>04/10/2024</b>	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.
<b>04/13/2023</b>	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.
<b>04/13/2022</b>	Policy reviewed, updated Overview, Summary, References. Updated policy name to include Topical Oxygen Therapy.
<b>04/05/2021</b>	Policy reviewed, no changes to criteria. Updated references.
<b>04/23/2020</b>	Policy reviewed, no changes to criteria.
<b>06/19/2019</b>	Policy reviewed, no changes to criteria.
<b>03/08/2018</b>	Policy reviewed, no changes to criteria.
<b>12/16/2009</b>	MCR no longer scheduled for revision.
<b>04/30/2008</b>	New policy.

## REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. Local coverage determination for topical oxygen therapy (L37873). Effective date May 6, 2019. Revision effective May 4, 2023. Accessed February 19, 2025. <https://www.cms.gov/medicare-coverage-database/search.aspx>
2. 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.
3. Rayman G, Vas P, Dhatariya K, et al. Guidelines on use of interventions to enhance healing of chronic foot ulcers in diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev*. 2020 Mar;36 Suppl 1:e3283. doi: 10.1002/dmrr.3283. PMID: 32176450.
4. 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.
5. Undersea and Hyperbaric Medical Society (UHMS). UHMS position statement: Topical oxygen for chronic wounds. Published 2005. Revised May 23, 2018. Accessed February 12, 2025. <https://www.uhms.org/resources/featured-resources/position-statements.html>
6. 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>.