Prior Authorization Review Panel
MCO Policy Submission

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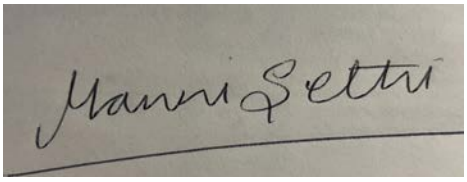
Plan: AmeriHealth Caritas Pennsylvania Community Health Choices	**Submission Date**: 1/1/2024
Policy Number: ccp.1182	**Effective Date:** 1/2016 **Revision Date:** December 1, 2023
Policy Name: Topical oxygen therapy	
Type of Submission – Check all that apply: **New Policy** **x Revised Policy*** **Annual Review – No Revisions** **Statewide PDL**	
***All revisions to the policy must be highlighted using track changes throughout the document.** **Please provide any clarifying information for the policy below:** See tracked changes below.	
Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Topical oxygen therapy

Clinical Policy ID: CCP.1182

Recent review date: 12/2023

Next review date: 4/2025

Policy contains: chronic wound care, diabetic foot ulcer, pressure ulcer, topical oxygen, non-healing wounds, venous ulcer.

AmeriHealth Caritas Pennsylvania Community HealthChoices has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania Community HealthChoices when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania Community HealthChoices will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are not guarantees of payment.

Coverage policy

Topical oxygen therapy is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Debridement of necrotic tissue.
- Revascularization surgery.
- Mechanical offloading.
- Blood glucose management.
- Foot care education.
- Mechanical compression.
- Limb elevation.
- Saline-moistened cotton gauze (wet-to-moist) dressing.
- Advanced dressings (e.g., hydrocolloid, foam, film, alginate, hydrofiber, hydrogel sheets, and collagen-based dressings).

- Full-body hyperbaric oxygen therapy.

Background

Chronic wounds represent a significant and growing health burden in the United States. In 2014, a total of 8.2 million (15%) Medicare beneficiaries had one type of wound or infection, not including pneumonia. The total cost of treating these wounds and infections was $28.1 to $31.7 billion (Nussbaum, 2018). Rising health care costs, an aging population, and a sharp rise in the incidence of diabetes and obesity worldwide are the main contributors to this growing burden.

The presence of oxygen is necessary for normal wound healing. A disrupted or compromised vasculature surrounding the wound can limit the oxygen supply and increase oxygen demands used to fight infection and repair tissue. This can lead to extreme tissue hypoxia. Noninvasive measurement of transcutaneous oxygen pressure applied to the skin of adjacent areas of a wound is used to estimate the oxygen tension of the wound (Oropallo, 2023).

Common chronic skin and soft tissue wounds include diabetic foot ulcers, pressure ulcers, and venous stasis ulcers of the lower extremity. Other chronic wounds include radiation ulcers caused by the acute or chronic effects of ionizing radiation. The injury may involve the skin, underlying soft tissue, and even deep structures, such as bone.

Oxygen has been offered as a therapeutic modality to assist and hasten wound healing. Introduced in the 1960s, systemic hyperbaric oxygen therapy increases the concentration of dissolved oxygen in the blood plasma, thereby enhancing the amount of oxygen perfusion in body tissues. The evidence suggests some effectiveness of hyperbaric oxygen therapy for treating chronic wounds, although confirmation from comparative effectiveness research is needed (Greer, 2013; Hoggan, 2014; O'Reilly, 2013; Stoekenbroek, 2014). The lack of availability of hyperbaric oxygen therapy facilities, contraindications to its use, patient transfer requirements, and the risk of undesired systemic side effects limit its use. Pressurized topical oxygen therapy was introduced to address these limitations.

Topical oxygen therapy administers pure oxygen to the wound area using a portable inflatable device that encases the limb at normobaric conditions or at a pressure slightly greater than atmospheric pressure. Unlike hyperbaric oxygen therapy, the effectiveness of topical oxygen therapy is independent of the wound's microcirculation. Other purported advantages are lower costs, a potentially lower risk of oxygen toxicity, and the possibility of home treatment (Handan, 2015).

The U.S. Food and Drug Administration classifies topical oxygen therapy as an oxygen chamber for extremities, which is intended to surround a patient's limb and apply humidified oxygen topically. This is performed at a pressure slightly greater than atmospheric pressure to aid in the healing of chronic skin ulcers. It is designated as a class II device with special controls, i.e., premarket notification (510k) requirements. Several devices have been approved for commercial use (U.S. Code of Federal Regulations, 21CFR878.5650, 2023; U.S. Food and Drug Administration, 2023).

The U.S. Food and Drug Administration has approved topical oxygen therapy for chronic skin ulcerations due to diabetes, venous stasis, postsurgical infections, gangrenous lesions, and decubitus ulcers; amputations/infected stumps; skin grafts; burns; and frostbite. Disposable, single-use devices are self-administered, which permits at-home use (Copeland, 2017).

Findings

The most recent guideline from the International Working Group on the Diabetic Foot recommends against using topical oxygen therapy as a primary or adjunctive intervention in diabetic foot ulcers including those that are difficult to heal (Rayman, 2020). Their findings were based on conflicting results from two randomized controlled trials.

Since then, an updated guideline from the Working Group has issued a conditional recommendation for topical oxygen as an adjunct to standard wound care, where standard of care alone has failed and resources exist to support this intervention. The Group's recommendation was based on low certainty evidence from three double-blinded, randomized controlled trials. One trial was terminated early, and the other two trials showed conflicting results. The group agreed that, on balance, the treatment effects favored use of topical oxygen with a moderate benefit on achieving absolute wound healing and reduction in ulcer area. There was no evidence for reduction in amputation up to 12 weeks. However, undesirable effects were poorly reported, although likely trivial based on expert opinion, and cost effectiveness data were lacking. Different devices were used to deliver topical oxygen, and the superiority of any one device could not be determined (Chen, 2023).

No other recent guideline endorses topical oxygen therapy using U.S. Food and Drug Administration-approved products.

Since 2016, four randomized controlled trials (n = 494) have been conducted in the United States. A systematic review of these trials examined the effectiveness of standard wound care with and without adjunctive topical oxygen therapy for chronic nonischemic diabetic foot ulcers (Wagner 1 and 2) and not adequately responding to standard wound care alone of at least four weeks duration. Each study was of 12 weeks duration, and different topical oxygen delivery systems were used. One trial was rated as low risk of bias, and the remaining three were rated as moderate risk of bias. Across studies, adverse events were similar in both study arms, but the absolute rates varied considerably. The differences in complete wound healing rates at 12 weeks ranged from 5% to 27%, favoring the topical oxygen therapy arm. In only one trial was the difference statistically significant. On meta-analysis, the difference between groups in the proportion of wounds healed at 12 weeks was significant (risk ratio = 1.59, 95% confidence interval 1.07 to 2.37, P = .021) (Carter, 2023).

Another systematic review and meta-analysis of seven randomized controlled trials (n = 614) found topical oxygen added to standard wound care resulted in higher complete healing rates than standard care alone (relative risk = 1.63, 95% confidence interval 1.33 to 2.00, P < .00001). Topical oxygen had no effect on the occurrence of adverse events, and its effect on reducing healing time was inconclusive. Limited follow up data for up to one year were available to determine recurrence or amputation rates, and direct evidence of improvement in healing durability or quality of life was lacking. Further studies are needed to confirm these findings (Sun, 2022).

A systematic review of 65 articles evaluated different oxygen therapies for promoting wound healing and found local oxygen therapy had more significant positive outcomes (63%). These outcomes promote the use of oxygen treatment in the stimulation of wound healing; however, the lack of clinical studies and vast methodological diversity made it impossible to perform a proper comparison within and between the different therapies (de Smet, 2017).

A systematic review of five studies of diabetics with chronic non-healing diabetic foot ulcers found topical oxygen achieved complete healing trajectory of wounds in low-grade (grade 1) ulcers, and either a 100% or 50% healing with reduction in ulcer size and tissue depth in high-grade ulcers. While the duration and application methods of topical oxygen therapy varied across studies, the investigators stated superior outcomes may be achieved with topical oxygen used as an adjunct to standard wound care, off-loading footwear, and proper wound bed dressing (Nataraj, 2019).

A large-scale review included charts of 3,462 patients, representing care of 4,127 total wounds with topical oxygen therapy from 2007 to 2016. The purpose of study was to assess the efficacy of topical oxygen therapy in healing chronic wounds in the home setting. All wounds were at least one square centimeter and treated with topical oxygen for at least two weeks. Participants were mostly Medicare and Medicaid enrollees (42.3% and 35.6%, respectively). The most common location of wounds was the foot (46%); of foot and toe wounds, about half were diabetes-related. The noncompliance rate was 4.1%. A majority (59.4%) of wounds experienced a reduction in size, with 27.5% completely healed. Median wound size decreased from 6 to 2 square centimeters. The proportion of cases with the largest (> 16 square centimeters) wounds fell from 24.4% to 16.2% after treatment. The greatest healing benefit occurred in chronic wounds that were smaller, less than one year old, and exposed to a longer treatment duration. The overall amputation rate for wounds treated with topical oxygen therapy was 2.4% (Copeland, 2017).

A systematic review/meta-analysis of six randomized controlled trials (n = 530) with a diabetes-related foot ulcer found topical oxygen therapy significantly increased the likelihood of ulcer healing compared to controls, regardless of whether the risk of study bias was high or low (Thanigaimani, 2021).

A systematic review/meta-analysis of eight studies of diabetic foot ulcer treatment showed that ulcers are more than twice as likely to heal after topical oxygen therapy than versus standard care alone (P = .00001). One study reported that time to 50% ulcer closure was shorter after topical oxygen versus sham (mean 18.4 versus 28.9 days, P = .001). However, the validity of most studies was low, and authors suggest more randomized trials (Connaghan, 2021).

Other controlled studies compared outcomes for patients treated with topical oxygen therapy and with another therapy. The largest of these recent controlled trials found superior outcomes in topical oxygen therapy patients, in terms of the proportion of patients with completely healed wounds, speed of wound healing, and low number of wound recurrences.

These assessments include:

- A group of 220 subjects with chronic diabetic foot ulcers found topical oxygen therapy was superior to sham treatment, with closure rates of 41.7% versus 13.5% after 12 weeks of treatment (P = .01, and P = .004 after adjustment for ulcer grade). A significant difference (56% versus 27%, P = .013) was also observed in the proportion of active arm ulcers that were closed after 12 weeks (Frykberg, 2020).
- A randomized controlled trial (n = 145) analyzed outcomes for participants with diabetic foot ulcers (grade 1-2) or minor amputation wounds after standard care with or without topical oxygen therapy for 12 weeks. Combination therapy resulted in significantly greater rates of healing (44.4% versus 28.1%, P = .044), and reduction in wound area (70% versus 40%, P = .005). No differences between groups in pain levels and adverse events were observed (Serena, 2021).
- A study of participants with chronic traumatic wounds (n = 112) compared negative-pressure wound therapy with or without topical oxygen. In patients receiving topical oxygen therapy, significant (P < .05) improvements occurred in Pressure Ulcer Scale for Healing scores; coverage rate of granulation tissue; bacterial culture-positive rate; VAS scores; and Transcutaneous Oxygen Partial Pressure. After three months, the wound healing rate was higher and the healing time shorter in the topical oxygen therapy group (P < .05) (Song, 2021).
- A study of 202 Veterans Administration hospital participants with diabetic foot ulcers compared results of standard treatments with versus without topical wound oxygen therapy. Those with oxygen therapy had an 88% lower rate of hospitalizations (6.6% versus 54.1%) and a 71% lower rate of amputations (12.1% versus 41.4%) within 360 days, both significant at P < .0001 (Yellin, 2021).

In 2022, we updated the references and deleted several older references that were analyzed in the included systematic reviews or have been archived. No policy changes are warranted.

In 2023, we added a guideline update (Chen, 2023) and two systematic reviews (Carter, 2023; Sun, 2022) to the policy. No policy changes are warranted.

References

On September 28, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “continuous diffusion of oxygen,” “transcutaneous oxygen therapy,” “topical oxygen,” “chronic wound,” and “diabetic ulcer.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

8/2015: initial review date and clinical policy effective date: 1/2016

8/2016: Policy references updated.

8/2017: Policy references updated.

8/2018: Policy references updated.

12/2019: Policy references updated. Policy ID changed to CCP.1182.

12/2020: Policy references updated.

12/2021: Policy references updated.

12/2022: Policy references updated.

12/2023: Policy references updated.