Clinical Policy Title: Topical oxygen therapy

Clinical Policy Number: 16.02.05

Effective Date: January 1, 2016
Initial Review Date: August 19, 2015
Most Recent Review Date: August 17, 2016
Next Review Date: August 2017

Related policies:

CP# 16.03.01 Bioengineered skin substitutes for ulcers and wound care
CP# 16.02.02 Growth factors for wound healing
CP# 16.03.03 Negative pressure wound therapy
CP# 18.02.01 Full body hyperbaric oxygen therapy (HBOT)

ABOUT THIS POLICY: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania's 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 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’s clinical policies are for informational purposes only and not intended as medical advice or direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Pennsylvania considers the use of topical oxygen therapy to be investigational and, therefore, not medically necessary.

Limitations:

All other uses of topical oxygen therapy are not medically necessary.

Note: The following CPT/HCPCS codes are not listed in the Pennsylvania Medicaid fee schedule:

A4575 - Topical hyperbaric chamber, disposable
E0446 - Topical Oxygen Delivery System, not otherwise specified, includes all supplies and accessories

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 U.S., affecting approximately 6.5 million patients and costing in excess of 25 billion dollars annually (in 2009 dollars). Increasing health care costs, an aging population, and a sharp rise in the incidence of diabetes and obesity worldwide are the main contributors to this increasing burden (Sen, 2009).

When healthy tissue is wounded, acute wounds generally proceed through an orderly reparative process that results in a durable restoration of anatomic and functional integrity (Sen, 2009). However, various physiologic and mechanical factors may impair the healing response, resulting in a chronic wound that fails to proceed through the usual process, or persists despite appropriate care. The most common culprits are local infection, trauma, foreign bodies, systemic problems such as diabetes mellitus, malnutrition, immunodeficiency, certain medications, and hypoxia (Sen, 2009).

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. Non-invasive measurement of transcutaneous oxygen pressure (PtcO2) applied to the skin of adjacent areas of a wound is used to estimate the oxygen tension of the wound. Tissue hypoxia is defined as a PtcO2 <40 mm Hg (Schreml, 2010; Fife, 2009).

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.

Treatment of chronic wounds

Wound care comprises nonsurgical and surgical methods and depends on the type and stage of the wound. According to the Association for the Advancement of Wound Care (AAWC), successful medical management relies on addressing the underlying cause of the wound and the following key principles (AAWC, 2010 a and b):

- Adequate debridement of necrotic and devitalized tissue.
- Control of infection.
- Wound dressing to promote a clean, healing wound with granulation tissue.
- Pain management.
- Nutritional supplementation.
When ulcers fail to respond adequately to standard treatment, advanced interventions are available depending on ulcer type. They include: electrical stimulation, negative pressure wound therapy, therapeutic ultrasound, ultraviolet (UV) light or multi-wavelength phototherapy, growth factors, infrared or monochromatic light stimulation, and split-thickness skin grafting or bioengineered skin (Gottrup, 2012; AAWC, 2010 a and b).

Oxygen has been offered as a therapeutic modality to assist and hasten wound healing. Introduced in the 1960s, systemic hyperbaric oxygen therapy (HBOT) increases the concentration of dissolved oxygen in the blood plasma, thereby enhancing the amount of oxygen perfusion in body tissues. HBOT delivers 100 percent oxygen at two to three atmospheres of pressure over the course of 60 – 120 minutes, in a specialized patient chamber. The number of treatments may range from 10 – 30. The evidence suggests some effectiveness of HBOT for treating chronic wounds, although confirmation from comparative effectiveness research is needed (Hoggan, 2014; Stoekenbroek, 2014; O’Reilly, 2013; Greer, 2013). The availability of HBOT 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:**

Topical oxygen therapy (TO2) administers pure oxygen to the wound area using a portable inflatable device that encases the limb at a pressure slightly greater than atmospheric pressure. Unlike HBOT, the effectiveness of TO2 is independent of the wound’s microcirculation. Other advantages are lower costs, a potentially lower risk of oxygen toxicity, and the possibility of home treatment. The U.S. Food and Drug Administration (FDA) classifies TO2 as a topical oxygen chamber for extremities (TOCE), 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 (U.S. Code of Federal Regulations, 21CFR878.5650).

**Searches**

AmeriHealth Caritas Pennsylvania searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 1, 2016. Search term was “topical oxygen therapy.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
• **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

We identified three systematic reviews (Greer, 2012; CADTH, 2012; Hayes, 2002), six evidence-based guidelines (Qaseem, 2015; O’Donnell, 2014; Lipsky, 2012; Bakker, 2012; AAWC, 2010a and b) and no economic analyses for this policy.

There are also several controlled studies comparing outcomes for patients treated with TO2 and with another therapy. One early study showed that slower healing occurred in patients given TO2 (Leslie, 1988). More recent controlled trials found superior outcomes in TO2 patients, in terms of proportion of patients with completely healed wounds, speed of wound healing, and low number of wound recurrences. These include a study of wound patients comparing TO2 to hyperbaric oxygen therapy (Gordillo, 2008), a study of refractory venous ulcers comparing TO2 to compression dressing (Tawfick, 2009), and a study of diabetic foot ulcer patients comparing TO2 to silver containing dressing changes (Blackman, 2010). Other observational reports found positive outcomes in patients treated with TO2, although they are not compared to subjects receiving other therapies (Landau, 1998; Heng, 2000; Kalliainen, 2003).

There may be variations of TO2 therapy that can more effectively improve treatments in the future. One report examined oxygen-generating wound dressings using sodium percarbonate (SPO) and calcium peroxide (CPO) as chemical oxygen sources, with positive early results (Chandra, 2015).

The overall quality of the evidence is low with a high risk of bias because of small sample sizes, the inclusion of different wound types and patient ages, additionally applied wound care regimens, non-standardized treatment protocols, and a poor evaluation of comorbidities. The current evidence is insufficient to support the effectiveness of TO2 for the treatment of chronic wounds. According to the Undersea Hyperbaric Medicine Society (UHMS), mechanisms of action for HBOT and TO2 are not similar and the mechanisms of action whereby TO2 might be effective or toxic have not been clearly defined (Feldmeier, 2005). Systematic reviews noted incomplete reporting of adverse effects, but when reported, adverse effects were rare. Evidence of TO2 toxicity included endothelial cell damage and reduced vascularization, due to extended topical exposure to pure gaseous oxygen. Both adverse effects reversed spontaneously after cessation of therapy, and the potential for the pressurized bag sealed around the extremity to exert a tourniquet-like effect on perfusion.

The evidence is inconclusive regarding the healing effects of TO2 on chronic wounds of any type. While most observational studies reported some evidence of improved wound healing with TO2, evidence from the most completely randomized trial did not demonstrate a beneficial effect for TO2 in patients with diabetic foot ulcers. Evidence-based guidelines either do not support or mention the use of TO2 in advanced wound care. Unlike systemic HBOT, where a large body of supportive basic and clinical research has been conducted, there is no similar body of background research for TO2. Large, well-designed randomized controlled trials (RCTs) with standardized protocols are needed to determine if TO2 provides any benefit to patients with chronic wounds, either alone or as an adjunct to standard wound care.

**Policy updates:**
A review of the peer-reviewed medical literature resulted in the addition of 14 new references, three of which were added to the summary of clinical evidence section.

### Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, methods, recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Greer (2012)</strong></td>
<td>Key points:</td>
</tr>
</tbody>
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| For VA Quality Enhancement Research Initiative (QUERI) | - Systematic review of advanced wound care therapy RCTs.  
- No RCTs for TO2 found.  
- Insufficient evidence of effectiveness. |
| **CADTH (2012)**                | Key points:                       |
| Systematic review of studies comparing TO2 to HBOT or standard care | - Three observational studies (2006 – 11), including one prospective controlled single-center study and two parallel observational studies.  
- Overall quality: low with high risk of bias. No randomization or blinding.  
- Observational studies show TO2 healed ~80% of diabetic foot ulcers (DFU), refractory venous ulcers (RVU), and chronic wounds without recurrence. No direct comparisons between TO2 or HBOT or standard care. No evidence of cost-effectiveness. |
| **Blackman (2010)**             | Key points:                       |
| Comparing topical oxygen therapy with silver containing dressing changes | - Prospective controlled study of 28 outpatients with diabetic foot ulcers.  
- 17 treated with topical oxygen therapy, 11 with silver containing dressing changes.  
- In oxygen group, more healed completely (82.4% vs. 45.5%) and quicker (average 56 days vs. 93 days).  
- No adverse events observed, no recurrence at ulcer site after 24 months. |
| **Tawflick (2009)**             | Key points:                       |
| Comparing topical oxygen therapy with compression dressings | - 83 patients with refractory venous ulcers.  
- 46 patients given topical oxygen therapy, 37 given compression dressings.  
- At 12 weeks, more oxygen patients fully healed (80% vs. 35%)  
- After one year follow-up, none of healed oxygen patients had recurrence; five of 13 compression dressing patients had recurrence. |
| **Gordillo (2008)**             | Key points:                       |
| Comparing topical oxygen therapy with hyperbaric oxygen therapy | - 1,854 patients screened in outpatient wound clinic.  
- 25 given portable topical oxygen therapy, 32 given hyperbaric oxygen therapy.  
- Topical group had significantly improved wound size vs. hyperbaric group.  
- Topical oxygen group associated with higher expression in healing wounds among the three oxygen-sensitive genes. |
| **Hayes (2002)**                | Key points:                       |
| Systematic review of three studies comparing TO2 to other treatments | - One small RCT of TO2 as an adjunct to standard wound care; one incomplete RCT of TO2 as a primary therapy, and one uncontrolled study.  
- Overall quality: low with high risk of bias.  
- TO2 is generally safe. Reported complications: endothelial cell damage and reduced vascularization due to extended topical exposure to pure gaseous oxygen, which reversed spontaneously after cessation of therapy; pressurized bag sealed around an extremity can exert a tourniquet-like effect.  
- Possible beneficial effect but inconclusive evidence that TO2 enhances the rate of wound healing in patients with chronic, necrotic, or gangrenous wounds. |
**Glossary**

**Debride (or debridement)** — To surgically excise dead, devitalized, or contaminated tissue; remove foreign matter from a wound.

**Diabetic foot ulcer** — An open sore or wound that occurs in approximately 15 percent of patients with diabetes and is commonly located on the bottom of the foot.

**Granulation** — Minute red granules of new capillaries formed on the surface of a wound in healing.

**Granulation tissue** — Highly vascularized tissue that replaces the initial fibrin clot in a wound.

**Chronic wounds** — Wounds that have failed to proceed through an orderly and timely reparative process to produce anatomic and functional integrity of the injured site.

**Pressure ulcer** — Also called decubitus ulcer or pressure sore, this is an area of unrelieved pressure over a defined area, usually over a bony prominence, resulting in ischemia, cell death, and tissue necrosis. It is common among patients hospitalized in acute and chronic care facilities.

**Venous ulcer** — Also called venous insufficiency ulceration, stasis ulcers, stasis dermatitis, varicose ulcers, or ulcus cruris. A chronic wound caused by inadequate blood flow through the veins, usually of the legs. They are the major occurrence of chronic wounds, occurring in 70 percent to 90 percent of leg ulcer cases.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


Clinical trials:

Searched clinicaltrials.gov on June 10, 2016 using term “topical oxygen therapy.” | Open Studies. Four studies found, one relevant.

CMS National Coverage Determination (NCDs):

Hyperbaric Oxygen Therapy (20.29). No Medicare coverage is made for application of topical oxygen. Available at: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=12&ncdver=3&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCD%7cMEDCAC%7cTA%7cMCD&PolicyType=Final&s=All&KeyWord=oxygen&KeyWordLookUp=Doc&KeyWordSearchType=And&CptHcpcsCode=A4575&kq=true&bc=IAAAAAAABAAAAAA%3d%3d&. Accessed August 1, 2016.

Local Coverage Determinations (LCDs):


Commonly submitted codes
Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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