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 19, 2015
Next Review Date: August, 2016

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: Arbor Health Plan has developed clinical policies to assist with making coverage determinations. Arbor Health Plan’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 Arbor Health Plan 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. Arbor Health Plan’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. Arbor Health Plan’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Arbor Health Plan will update its clinical policies as necessary. Arbor Health Plan’s clinical policies are not guarantees of payment.

Coverage policy

[Arbor Health Plan 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 codes are not listed in the Nebraska 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 or 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 2010a & 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 2010a & b).

Oxygen has been offered as a therapeutic modality to assist and hasten wound healing. Introduced in the 1960s, systematic 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 limits 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) (21CFR878.5650).

**Searches**
Arbor Health Plan 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 June 11, 2015. Search terms were "topical oxygen therapy," "Oxygen/therapy" [Mesh]) and "Hyperbaric Oxygenation" [Mesh] and "topical."

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**

Arbor Health Plan 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 &b) and no economic analyses for this policy.

The evidence consists of: one small, randomized controlled trial (RCT) evaluating TO2 as an adjunct to standard wound care; one small, incompletely randomized trial evaluating TO2 as a primary therapy; and observational studies that indirectly compared TO2 to either HBOT or standard wound care in persons with chronic, necrotic, or gangrenous wounds.

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 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 extremity casing 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.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, methods, recommendations</th>
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| Greer (2012)                 | **Key Points:**  
  - Systematic review of advanced wound care therapy RCTs.  
  - No RCTs for TO2 found.  
  - Insufficient evidence of effectiveness.                                                                                                                                                                         |
| For VA Quality Enhancement Research Initiative (QUERI) |                                                                                                                                                                                                 |
| CADTH (2012)                 | **Key Points:**  
  - Systematic review of comparative studies published between January 1, 2006 and December 19, 2011. Three observational studies, including one prospective controlled single-center study and two parallel observational studies, comparing TO2 to HBOT (or standard care).  
  - Overall quality: low with high-risk of bias. No randomization or blinding.  
  - Observational studies suggest 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 were available. No evidence of cost-effectiveness.  
  - Results inconclusive.                                                                                                                                                                                                 |
| Hayes (2002) [updated 2007] | **Key Points:**  
  - Systematic review of one small RCT of TO2 as an adjunct to standard wound care; one incompletely 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.                                                                                                                                 |

**Other policies:**

<table>
<thead>
<tr>
<th>Organization</th>
<th>Policy</th>
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<tbody>
<tr>
<td>CMS</td>
<td>Non-covered.</td>
</tr>
<tr>
<td>Aetna</td>
<td>Aetna considers topical HBOT directly administered to the open wound, and limb-specific</td>
</tr>
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hyperbaric oxygen pressurization in small limb-encasing devices experimental and investigational because its efficacy has not been established through well-controlled clinical trials.

| UHC # 2011T0520D | Topical oxygen therapy is unproven for the treatment of wounds or ulcers. Published studies do not provide sufficient evidence that topical oxygen therapy enhances the rate of healing of chronic wounds or ulcers. Large, well-designed, randomized controlled trials of topical oxygen therapy are needed to determine if this treatment is beneficial for health outcomes in patients with chronic wounds. |
| IBX #07.00.09d | Topical oxygenation is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by a review of the available published literature. |

**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, 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. The Pressure ulcers/wound classifications, according to the National Pressure Ulcer Advisory Panel (NPUAP) are as follows:

- **Stage I** — Intact skin with non-blanchable (does not turn white) redness of a localized area, usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area. The area may be painful, firm, soft, warmer or cooler as compared to adjacent tissue.

- **Stage II** — Partial thickness skin loss presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled blister. Bruising indicates suspected deep tissue injury. This stage should not be used to describe skin tears, tape burns, perineal dermatitis, maceration or excoriation.

- **Stage III** — Full thickness tissue loss. Subcutaneous fat may be visible; however, bone, tendon and/or muscles are not exposed. Slough may be present but does not obscure the depth of
tissue loss. May include undermining and tunneling. The depth of a stage III ulcer varies by anatomical location. The bridge of the nose, ear, occiput (the back part of the head or skull) and malleolus (the bony protuberance on either side of the ankle) do not have subcutaneous tissue and stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep stage III pressure ulcers. Bone/tendon is not visible or directly palpable.

- **Stage IV** — Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed, which often includes undermining and tunneling. The depth of a stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and these ulcers can be shallow. Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis possible. Exposed bone/tendon is visible or directly palpable.

- **Unstageable/Unclassified** — Full thickness skin or tissue loss, depth unknown. Full thickness tissue loss in which the actual depth of the ulcer is completely obscured by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed. Until enough slough and/or eschar are removed to expose the base of the wound, the true depth cannot be determined. However, it will be either a stage III or IV classification. Stable (dry, adherent, intact without erythema or fluctuance) eschar on the heels, serves as “the body’s natural (biological) cover” and should not be removed.

- **Suspected deep tissue injury** — Depth unknown. Purple or maroon localized area of discolored intact skin or blood-filled blister, due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue. Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid, exposing additional layers of tissue, despite optimal treatment.

**Venous ulcer** — Also called venous insufficiency ulceration, stasis ulcers, stasis dermatitis, varicose ulcers or ulcer 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.

**Related policies**

Arbor Health Plan Utilization Management program description.

**References**

**Professional society guidelines/other:**
Association for the Advancement of Wound Care (AAWC) venous ulcer guideline. 

Association for the Advancement of Wound Care (AAWC) guideline of pressure ulcers. 


Peer-reviewed references:

21CFR878.5650. Topical oxygen chamber for extremities. .


Canadian Agency for Drugs and Technologies in Health (CADTH). Rapid Response Report. Topical Oxygen


**Clinical trials:**

NCT02313428  Topical Oxygen Therapy for Diabetic Foot Ulcers.

NCT01913704 Pilot Study Comparing NatroxTM Topical Oxygen Therapy to A Placebo in the Management of Non-Healing Leg Ulcers.


**CMS National Coverage Determination (NCDs):**


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=IAAAABAAAAAAA%3d%3d&.

**Local Coverage Determinations (LCDs):**

L11446 Oxygen and Oxygen Equipment Oxygen and Oxygen Equipment.

L11457 Oxygen and Oxygen Equipment Oxygen and Oxygen Equipment.

L11468 Oxygen and Oxygen Equipment Oxygen and Oxygen Equipment.
L27221 Oxygen and Oxygen Equipment.

**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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<thead>
<tr>
<th>CPT Code</th>
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<tbody>
<tr>
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<table>
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<tr>
<th>ICD-9 Code</th>
<th>Description</th>
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<tr>
<td>454.0</td>
<td>Venous ulcer</td>
<td></td>
</tr>
<tr>
<td>707.0</td>
<td>Pressure ulcer</td>
<td>Add 5th digit for location</td>
</tr>
<tr>
<td>707.1</td>
<td>Ulcer of lower limb, except pressure ulcer</td>
<td>Add 5th digit for location</td>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>E11.622</td>
<td>Type II DM with skin ulcer</td>
<td>Use additional code for site</td>
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<tr>
<td>I83.009</td>
<td>Varicose vein, lower extremity with ulcer, site unspecified</td>
<td></td>
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<tr>
<td>L89.90</td>
<td>Pressure ulcer unspecified site, unspecified stage</td>
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<thead>
<tr>
<th>HCPCS Level II</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>A4575</td>
<td>Topical hyperbaric chamber, disposable</td>
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