Hyperbaric oxygen therapy (HBOT) involves breathing 100% oxygen at a pressure of more than 1 atmosphere (atm). It is generally applied systemically with the patient inside a hyperbaric chamber. It can also be applied topically; that is, the body part to be treated is isolated, e.g., in an inflatable bag and exposed to pure oxygen.

HBOT is a technique of delivering higher pressures of oxygen to the tissues. Two methods of administration are available. In systemic or large hyperbaric oxygen chamber, the patient is entirely enclosed in a pressure chamber and breathes oxygen at a pressure greater than 1 atmosphere (atm; the pressure of oxygen at sea level). Thus, this technique relies on systemic circulation to deliver highly oxygenated blood to the target site, typically a wound. In addition, systemic HBOT can be used to treat systemic illness, such as air or gas embolism, carbon monoxide poisoning, clostridial gas gangrene. Treatment may be carried out either in a monoplace chamber pressurized with pure oxygen or in a larger, multiplace chamber pressurized with compressed air, in which case the patient receives pure oxygen by mask, head tent, or endotracheal tube.

Topical HBOT is a technique of delivering 100% oxygen directly to an open, moist wound at a pressure slightly higher than atmospheric pressure. It is hypothesized that the high concentrations of oxygen diffuse directly into the wound to increase the local cellular oxygen tension, which in turn promotes wound healing. Topical HBO devices consist of an appliance to enclose the wound area (frequently an extremity) and a source of oxygen; conventional oxygen tanks may be used. The appliances may be disposable and may be used without supervision in the home by well-trained patients.

Related Policies

- N/A

Policy

Topical hyperbaric oxygen therapy is considered investigational.

Systemic hyperbaric oxygen pressurization may be considered medically necessary in the treatment of any of the following conditions:

- Acute carbon monoxide poisoning
- Acute cyanide poisoning
- Acute gas embolism
- Acute traumatic ischemia (e.g., crush injuries, reperfusion injury, compartment syndrome)
- Chronic refractory osteomyelitis
• Decompression sickness
• Gas gangrene (i.e., clostridial myonecrosis)
• Non-healing diabetic wounds of the lower extremities in patients who meet all of the following criteria:
  o Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes
  o Patient has a wound classified as Wagner grade 3 or higher (see Policy Guidelines)
  o Patient has no measurable signs of healing after 30 days of an adequate course of standard wound therapy
• Pre- and post-treatment for patients undergoing dental surgery (non-implant related) of an irradiated jaw
• Profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed
• Soft-tissue radiation necrosis (e.g., radiation enteritis, cystitis, proctitis) and osteoradionecrosis

Hyperbaric oxygen pressurization is considered investigational in all other situations, included but not limited to, the treatment of the following conditions:

• Acute carbon tetrachloride poisoning
• Acute cerebral edema
• Acute coronary syndromes and as an adjunct to coronary interventions, including but not limited to, percutaneous coronary interventions and cardiopulmonary bypass
• Acute ischemic stroke
• Acute osteomyelitis
• Acute peripheral arterial insufficiency
• Acute retinal artery insufficiency
• Acute surgical and traumatic wounds
• Acute thermal burns
• Autism spectrum disorders
• Bell's palsy
• Bisphosphonate-related osteonecrosis of the jaw
• Bone grafts
• Brown recluse spider bites
• Cerebral palsy
• Cerebrovascular disease, acute (thrombotic or embolic) or chronic
• Chronic arm lymphedema following radiotherapy for cancer
• Chronic wounds, other than those in patients with diabetes who meet the criteria specified in the medically necessary statement
• Compromised skin grafts or flaps
• Delayed onset muscle soreness
• Demyelinating diseases (e.g., multiple sclerosis, amyotrophic lateral sclerosis)
• Early treatment (beginning at completion of radiotherapy) to reduce adverse effects of radiotherapy
• Fracture healing
• Herpes zoster
• Hydrogen sulfide poisoning
• Idiopathic femoral neck necrosis
• Idiopathic sudden sensorineural hearing loss (ISSNHL)
• In vitro fertilization
• Inflammatory bowel disease (Cohn’s disease or ulcerative colitis)
• Intra-abdominal and intracranial abscesses
• Lepromatous leprosy
• Meningitis
• Migraine
• Motor dysfunction associated with stroke
• Necrotizing soft tissue infections
• Pseudomembranous colitis (antimicrobial agent-induced colitis)
• Pyoderma gangrenosum
• Radiation-induced injury in the head and neck
• Radiation myelitis
• Radiation-induced injury in the head and neck, except as noted earlier in the medically necessary statement
• Refractory mycoses: mucormycosis, actinomycosis, conidiobolus coronato
• Retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment
• Senility related disorders including dementia, vascular dementia, and cognitive impairment
• Sickle cell crisis and/or hematuria
• Spinal cord injury
• Traumatic brain injury
• Tumor sensitization for cancer treatments, including but not limited to, radiotherapy or chemotherapy
Policy Guidelines

**Topical Hyperbaric Oxygen**

HCPCS code A4575 is used to describe the disposable appliance that is positioned around the wound area. Conventional oxygen tanks, typically gas, are used to supply the oxygen.

Topical hyperbaric oxygen (HBO) may be performed in the office, clinic, or may be self-administered by the patient in the home. Typically, the therapy is offered for 90 minutes per day for 4 consecutive days. After a 3-day break, the cycle is repeated. The regimen may last for 8 to 10 weeks.

**Systemic Hyperbaric Oxygen**

The Wagner classification system of wounds is defined as follows:

- Grade 0: no open lesion
- Grade 1: superficial ulcer without penetration to deeper layers
- Grade 2: ulcer penetrates to tendon, bone, or joint
- Grade 3: lesion has penetrated deeper than grade 2 and there is abscess, osteomyelitis, pyarthrosis, plantar space abscess, or infection of the tendon and tendon sheaths
- Grade 4: wet or dry gangrene in the toes or forefoot
- Grade 5: gangrene involves the whole foot or such a percentage that no local procedures are possible and amputation (at least at the below the knee level) is indicated

Following are suggestions from the Undersea and Hyperbaric Medical Society’s (UHMS) 2008 Hyperbaric Oxygen Therapy Committee report on utilization of Hyperbaric oxygen therapy (HBOT) (Gesell, 2008):

- **Acute carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning:** Some patients improve after a single treatment. Patients who fail to demonstrate a full recovery should receive additional treatments. In patients with persistent neurologic dysfunction after the initial treatment, further treatment can occur within 6 to 8 hours and can be continued once or twice daily until there is no additional improvement in cognitive function. Utilization review is mandatory after the fifth treatment.

- **Acute gas embolism:** It is recommended that treatments continue until there is no additional improvement; this typically occurs after 1 to 2 treatments but occasionally up to 5 to 10. Utilization review is recommended after 10 treatments.

- **Chronic refractory osteomyelitis:** No recommendations were made for the total number of treatments required. For patients who respond to initial treatment with antibiotics, surgical débridement and HBO, therapy should be continued for approximately 4 to 6 weeks. Utilization review is indicated after 30 to 40 sessions.

- **Crush injury, compartment syndrome, and other acute traumatic ischemias:**
  - **Crush injury:** 8 treatments (three times per day for 2 days, then twice a day for 2 days and daily for 2 days)
  - **Compartment syndrome:** 3 treatments (twice a day for 1 day and 1 treatment on day 2)
  - **Reperfusion injury:** 1 treatment
• Decompression sickness: The majority of cases respond to a single treatment. Patients with residual defects after the initial session should receive additional treatments until they achieve clinical stability (generally no more than 5-10 treatments). Utilization review is recommended after 10 treatments.

• Enhancement of healing in problem wounds: Treatments are performed for 90 to 120 minutes. The initial treatment schedule depends on the severity of disease. More serious conditions may require twice daily treatments; when stabilized, this can decrease to once daily. Utilization review is required after the initial 30 days of treatment and at least once every additional 30 days.

• Gas gangrene (i.e., clostridial myonecrosis): Recommended are three 90-minute treatments during the first 24 hours and then 2 treatments per day for the next 2 to 5 days, depending on the patient’s initial response. Utilization review is indicated after 10 treatments.

• Mandibular osteoradionecrosis: The initial course of treatment for patients with stage 1 osteoradionecrosis is 30 sessions, followed by only minor bony débridement. If response is adequate, an additional 10 treatments are given. If patients are not responding, they are considered stage II and they receive more extensive surgical débridement, followed by 10 additional treatments. Patients who present as stage III patients receive 30 treatments followed by mandibular segmental resection and then an additional 10 treatments.

• Severe anemia: HBO can be considered for severe anemia when patients cannot receive blood products due to medical, religious, or strong personal preference reasons. Treatment can occur for periods of up to 3 or 4 hours 3 to 4 times a day if patients receive intratreatment air breaks. HBO treatment should be continued with taper of both time and frequency until red blood cells have been satisfactorily replaced by patient regeneration or the patient can undergo transfusion.

• Soft tissue radiation necrosis (e.g., radiation enteritis, cystitis, and proctitis) and osteoradionecrosis: Most treatment courses for radiation injury will be 30 to 60 treatments (once daily for 90 to 120 minutes). Utilization review is recommended after 60 treatments.

### Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.
Rationale

Background

HBOT is a technique of delivering higher pressures of oxygen to the tissues. Two methods of administration are available. In systemic or large hyperbaric oxygen chamber, the patient is entirely enclosed in a pressure chamber and breathes oxygen at a pressure greater than 1 atmosphere (atm; the pressure of oxygen at sea level). Thus, this technique relies on systemic circulation to deliver highly oxygenated blood to the target site, typically a wound. In addition, systemic HBOT can be used to treat systemic illness, such as air or gas embolism, carbon monoxide poisoning, clostridial gas gangrene. Treatment may be carried out either in a monoplace chamber pressurized with pure oxygen or in a larger, multiplex chamber pressurized with compressed air, in which case the patient receives pure oxygen by mask, head tent, or endotracheal tube.

Topical HBOT is a technique of delivering 100% oxygen directly to an open, moist wound at a pressure slightly higher than atmospheric pressure. It is hypothesized that the high concentrations of oxygen diffuse directly into the wound to increase the local cellular oxygen tension, which in turn promotes wound healing. Topical HBO devices consist of an appliance to enclose the wound area (frequently an extremity) and a source of oxygen; conventional oxygen tanks may be used. The appliances may be disposable and may be used without supervision in the home by well-trained patients. Topical HBOT has been investigated as a treatment of skin ulcerations resulting from diabetes, venous stasis, postsurgical infection, gangrenous lesion, decubitus ulcers, amputations, skin graft, burns, or frostbite.

Regulatory Status

In February 1999, the Numobag™ Kit (Numotech Inc., Woodland Hills, CA) for application of topical hyperbaric therapy was cleared for marketing by FDA through the 510(k) process. FDA determined that this device was substantially equivalent to existing devices. The most recent topical oxygen therapy delivery devices to be approved are the Natrox™ Topical Oxygen Delivery System (Inotec Amd Ltd.) and Epiflo® (Neogenix Llc). Both of these devices were approved in 2012. Product Code: KPJ.

In May 2005, the ATA Monoplace Hyperbaric System (ATA Hyperbaric Chamber Manufacturing Inc.) was cleared for marketing by FDA through the 510(k) process. FDA determined that this device was substantially equivalent to existing hyperbaric devices. Product Code: CBF.

In 2013, FDA published a statement warning that non-FDA approved uses of HBOT may endanger the health of patients. If patients mistakenly believe that HBOT devices have been proven safe for uses not cleared by FDA, they may delay or forgo proven medical therapies.

Topical Hyperbaric Oxygen

Due to their different methods of delivery, topical and systemic hyperbaric oxygen (HBO) are distinct technologies such that they must be examined separately. At the time of policy development, there was minimal published literature on topical hyperbaric oxygen therapy (HBOT). The literature primarily consists of case reports or small uncontrolled case series. There was 1 small randomized controlled trial (RCT) that included 18 patients with diabetic foot ulcers who were assigned to receive either topical HBOT plus standard wound care or standard wound care alone. Changes in ulcer size and depth did not differ between the 2 groups.
Systemic Hyperbaric Oxygen

The original policy on systemic HBO was based entirely on the 1996 guidelines published by the Undersea and Hyperbaric Medical Society (UHMS) and was subsequently revised in 1999 with 3 TEC Assessments. The TEC Assessments had conclusions similar to UHMS, except, in contrast to the UHMS guidelines, they stated that there was insufficient evidence to conclude that HBOT improved the net health outcome for the following indications:

- Compromised skin grafts
- Acute thermal burns
- Chronic refractory osteomyelitis
- Necrotizing soft tissue infections
- Brown recluse spider bites

The TEC Assessments also stated that there was insufficient evidence to permit conclusions on the use of HBO for treatment of brain injury, spinal cord injury, and Crohn’s disease, indications not addressed by the 1996 UHMS Guidelines. Literature updates have focused on identifying new RCTs and meta-analyses of RCTs, particularly on indications considered investigational at the time of the update.

Chronic Wounds

A Cochrane review of RCTs on HBO treatment for chronic wounds was published by Kranke et al in 2012. The authors identified 9 RCTs, with a total of 471 participants that compared the effect of HBOT on chronic wound healing with an alternative treatment approach that did not use HBOT. Eight of the 9 trials included in the review evaluated HBOT in patients with diabetes. The remaining trial addressed HBO for patients with venous ulcers, that study had only 16 participants and the comparator treatment was not specified. In a pooled analysis of data from 3 trials, a significantly higher proportion of ulcers had healed at 6 weeks in the group receiving HBO than the group not receiving HBOT (risk ratio [RR]=5.20; 95% confidence interval [CI]: 1.25 to 21.7). Pooled analyses, however, did not find statistically significant differences between groups in the proportion of ulcers healed at 6 months (2 trials) or 12 months (3 trials). There were insufficient data to conduct pooled analyses of studies evaluating HBOT for treating patients with chronic wounds who did not have diabetes.

In 2013, O’Reilly et al published a systematic review of studies on HBOT for treatment of diabetic ulcers. The authors identified 6 RCTs and 6 non-RCTs that compared HBOT with standard wound care or sham therapy in patients with diabetes who had nonhealing lower-limb ulcers. Pooled analyses of observational studies found statistically significant benefits of HBOT on rates of major amputation, minor amputation, and the proportion of wounds healed at the end of the study period. However, in pooled analyses of RCT data, the stronger study design, there were no statistically significant differences between groups on key outcomes. This included the rate of major amputation (RR=0.40; 95% CI: 0.07 to 2.23; p=0.29), minor amputation (RR=0.79; 95% CI: 0.19 to 3.30, p=0.75), and the proportion of unhealed wounds at the end of the study period (RR=0.54, 95% CI: 0.26 to 1.13, p=0.1).

A 2011 RCT conducted with diabetic patients was double-blind and included 75 diabetic patients with chronic wounds who had failed at least 2 months of treatment at a
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diabetic foot clinic.11 After 12 months, the healing rate was 61% in the HBOT group and 27% in the sham hyperbaric group; this difference was statistically significant (p=0.009).

Although at least some RCTs have found benefit, systematic reviews have had mixed findings on the impact of HBOT on diabetic ulcers. A Cochrane review found short-term, but not long-term benefit on wound healing, and a 2013 meta-analysis did not find significant benefits of HBOT on outcomes in RCTs, but did find an effect in non-RCTs. There is insufficient evidence on HBOT for treatment of chronic wounds in patients without diabetes.

**Acute Surgical and Traumatic Wounds**

In 2013, a updated Cochrane review of RCTs on HBOT for acute surgical and traumatic wounds was published by Eskes et al.12 HBOT was defined as use of 100% oxygen at pressures above 1 atm. To be included, studies needed to compare HBOT with a different intervention or compare 2 HBOT regimens; in addition, studies needed to objectively measure wound healing. A total of 4 met the review’s inclusion criteria. The studies ranged in size from 10 to 135 participants. Due to differences among studies in terms of patient population, comparison intervention, outcome measurement, etc., study results could not be pooled. The primary outcome examined by Cochrane reviewers, wound healing, was not reported in either of the 2 trials comparing HBOT with usual care and was not reported in the 1 trial comparing HBOT with dexamethasone or heparin. Complete wound healing was reported in the 1 RCT comparing active HBOT with sham HBOT. In this small study (n=36), there was a statistically higher rate of wound healing in the group; the time point for outcome measurement in this study was unclear. In the sham-controlled study, there was no statistically significant difference between groups in the mean time to wound healing.

Another 2014 systematic review of studies on HBOT for acute wounds, published by Dauwe et al, included RCTs and non-RCTs.13 The review included 8 studies, with sample sizes ranging from 5 to 125 patients. Four studies were randomized, 3 were prospective non-RCTs, and 1 was a retrospective non-RCT. As in the Eskes systematic review, data were not pooled. The authors noted that 7 of the 8 studies reported achieving statistical significance in their primary end points, but the end points differed among studies (e.g., graft survival, length of hospital stay, and wound size). Moreover, the studies were heterogeneous in terms of treatment regimens, patient indications (e.g., burns, face lifts), and study designs, making it difficult to draw conclusions about the effect of HBOT on acute wound treatment.

There is insufficient evidence supporting HBOT for treatment of acute wounds; additional evidence from high-quality RCTs is needed.

**Carbon Monoxide Poisoning**

A 2011 Cochrane review of 7 RCTs concluded that the available evidence is insufficient to determine whether adverse neurologic outcomes in patients with carbon monoxide poisoning are reduced with HBOT.14 In 2008, the American College of Emergency Physicians (ACEP) published a clinical policy on critical issues in carbon monoxide poisoning.15 Their literature review indicated there was only level C evidence (preliminary, inconclusive, or conflicting evidence) for treatment of acute carbon monoxide poisoning. The 2008 UHMS guidelines, however, lists carbon monoxide poisoning as an indication for HBOT.

Two blinded randomized trials were discussed in both the Cochrane and ACEP reviews. One is a study by Scheinkestel et al, a double-blind, RCT comparing HBOT with normobaric oxygen in patients with carbon monoxide poisoning.16 The authors reported
that HBOT did not benefit patient outcomes of neuropsychologic performance when HBOT was completed and at 1-month follow-up. This study was limited, however, by a high rate (46%) of patients who were lost to follow-up. Moreover, the trial has been criticized for administering 100% normobaric oxygen for at least 72 hours between treatments, which has been called a toxic dose of oxygen. The critiques also mention that there was an unusually high rate of neurologic sequelae after the treatment period, which could be due in part to the high dose of oxygen and/or the high rate of cognitive dysfunction in the study population (69% were poisoned by carbon monoxide through suicide attempts).

The other blinded trial, by Weaver et al, also compared hyperbaric and normobaric oxygen. Patients received either 3 sessions of HBOT or 1 session of normobaric oxygen plus 2 sessions of exposure to normobaric room air. The primary outcome was the rate of cognitive sequelae at 6 weeks. Cognitive function was assessed using a battery of neuropsychological tests. At the 6-week follow-up, the intention-to-treat analysis found that 19 of 76 (25.0%) in the HBOT group and 35 of 76 (46.1%) in the control group had cognitive sequelae; the difference was statistically significant (p=0.007). There was a high rate of follow-up at 6 weeks, 147 of 152 (97%) of randomized patients. Enrollment in the study was stopped early because an interim analysis found HBOT to be effective. A follow-up study, which included 147 patients from the randomized trial and 75 who had been eligible for the trial but had not enrolled, was published in 2007. Of the group treated with HBOT (n=75), cognitive sequelae were identified in 10 of 58 (17%) at 6 months and 9 of 62 (14%) at 12 months. Of the group not treated with HBOT (n=163), 44 of 146 (30%) at 6 months and 27 of 149 (18%) at 12 months had cognitive sequelae. (The follow-up rate was higher at 12 months because the investigators received additional funding for data collection.) Thus, in light of the clinical studies, including the limitations of trials noted earlier, and given the strong clinical support for this treatment (see Clinical Input section next), the use of HBOT for acute carbon monoxide poisoning may be medically necessary.

Radionecrosis and Osteoradionecrosis

A 2008 Cochrane review by Esposito et al reviewed the use of HBOT in patients requiring dental implants. The authors identified 1 randomized trial involving 26 patients. The authors concluded that despite the limited amount of clinical research available, it appears that HBOT in irradiated patients requiring dental implants may not offer any appreciable clinical benefits. They indicated that there is a need for more RCTs to ascertain the effectiveness of HBOT in irradiated patients requiring dental implants.

In 2012, Bennett et al published a Cochrane review on HBOT for late radiation tissue injury. The authors identified 11 RCTs; there was variability among trials, and study findings were not pooled for the primary outcomes of survival, complete resolution of necrosis or tissue damage, and improvement in a late effects symptom scale. In a pooled analysis of 3 studies, a significantly higher proportion of patients with osteoradionecrosis achieved complete mucosal cover after HBOT compared with controls (RR=1.30; 95% CI: 1.09 to 1.55). From their review of the literature, the authors concluded that data from small trials “suggest that for people with LRTI [late radiation tissue injury] affecting the head, neck, anus, and rectum, [HBO] is associated with improved outcome. HBOT also appears to reduce the chance of ORN [osteoradionecrosis] following tooth extraction in an irradiated field. There was no such evidence of any important clinical effect on neurological tissues. The application of HBOT to selected patients and tissues may be justified.”

In 2012, Shao et al in China published an RCT including 36 patients who had undergone radiotherapy for pelvic malignancies and had radiation-induced hemorrhagic cystitis.
Patients were randomized to treatment with hyaluronic acid (n=16) or HBOT (n=20). The hyaluronic acid group received weekly injections for the first month and monthly injections for the following 2 months. HBOT consisted of 30-minute sessions daily for 1 month. All patients completed the study. There were no statistically significant differences in outcomes, e.g., pain or voids per day 6, 12, or 18 months after treatment. For example, at 12 months after treatment, the number of voids per day was 8.9 in the hyaluronic acid group and 9.7 in the HBOT group (p>0.05). The study may have been underpowered to detect statistically significant differences between groups.

In summary, given the longstanding use of this technology, the existing literature base, and the Cochrane reviews previously noted, the use of HBOT for treatment of soft tissue and bone radiation necrosis and for pre- and posttreatment of dental surgery (non-implant-related) in an irradiated jaw may be considered medically necessary.

Bisphosphonate-Related Osteonecrosis of the Jaw

An unblinded RCT was published by Freiberger et al in 2012 on use of HBO as an adjunct therapy for patients with bisphosphonate-related osteonecrosis of the jaw.23 Forty-nine patients were randomly assigned to HBOT in addition to standard care (n=22) or standard care alone (n=27). Five patients in the standard care group received HBOT and 1 patient assigned to the HBOT group declined HBO. The investigators decided to do a per-protocol analysis (actual treatment received) because of the relatively large degree of crossover. Participants were evaluated at 3, 6, 12, and 18 months. Data were available on 46 patients; 25 received HBOT in addition to standard care and 21 received standard care alone. The primary outcome measure was change in oral lesion size or number. When change from baseline to last available follow-up was examined, 17 of 25 (68%) of HBO-treated patients had improvement in oral lesion size or number compared with 8 of 21 (38%) in the standard care group (p=0.043). When change from baseline to 6, 12, or 18 months was examined, there was no statistically significant difference between groups in the proportion of patients with improvement. In addition, the proportion of patients who healed completely did not differ significantly between groups at any time point. This single trial does not report consistent findings of benefit across outcome measures. It also has a number of methodologic limitations, e.g., unblinded, crossover, and analysis performed on a per-protocol basis rather than intention to treat. A disadvantage of the per-protocol analysis is that randomization is not preserved, and the 2 groups may differ on characteristics that affect outcomes. As a result, this trial is insufficient to conclude that HBOT improves health outcomes for patients with bisphosphonate-related osteonecrosis of the jaw.

Osteomyelitis

No prospective clinical trials on chronic refractory osteomyelitis or acute refractory osteomyelitis were identified in updated searches. The justification for the use of HBOT in chronic osteomyelitis has been primarily based on case series. Among the larger case series, Maynor et al reviewed the records of all patients with chronic osteomyelitis of the tibia seen at 1 institution.24 Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBO treatments (range, 6-99). Of the 26 patients with at least 2 years of follow-up after treatment, 21 (81%) remained drainage-free. Twelve of 15 (80%) with follow-up data at 60 months had remained drainage-free. A study by Davis et al reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution.25 Patients received HBO until the bone was fully recovered with healthy vascular tissue; this resulted in a mean of 48 daily treatments (range, 8-103). After a mean post-treatment follow-up of 34 months, 34 of 38 (89%) patients remained clinically free of infection (i.e., drainage-free and no tenderness, pain, or cellulitis). Success rates from several smaller case series, all conducted in Taiwan, are 12 of 13 (92%)
patients, 11 of 14 (79%) patients, and 13 of 15 (86%) patients. Given the high percentage of refractory patients in these series who had successful outcomes and the clinical support for HBOT as an option for chronic refractory osteomyelitis (see Clinical Input section next), the use of HBOT for chronic refractory osteomyelitis may be considered medically necessary. HBOT for acute osteomyelitis refractory to medical treatment may be considered investigational.

**Fracture Healing**

In 2012, Bennett et al published a Cochrane review on HBOT to promote fracture healing and treat nonunion fractures. The investigators did not identify any published RCTs on this topic that compared HBOT with no treatment, sham or another intervention and reported bony union as an outcome. Due to the lack of RCTs, it is not possible to conclude whether the use HBOT to promote fracture healing improves outcomes; therefore, the use of HBOT for this indication is considered investigational.

**Compromised Skin Grafts and Flaps**

In 2006, Friedman et al published a systematic review of literature on use of HBOT for treating skin flaps and grafts. No RCTs were found. The authors identified 2 retrospective case series on use of HBOT for clinically compromised skin grafts and flaps. The series had sample sizes of 65 and 26, respectively; both were published in the 1980s based on treatment provided in the 1970s and 1980s. Given the limited published data and lack of recent data, this indication remains investigational.

**Necrotizing Soft Tissue Infections**

A 2005 systematic review by Jallali et al evaluated the literature on HBOT as adjunctive therapy for necrotizing fasciitis. They did not identify any RCTs. There were only a few retrospective studies with small sample sizes and findings were inconsistent. The authors concluded that more robust evidence is needed before widespread use of HBOT is recommended. A 2009 retrospective cohort study compared outcomes in 48 patients at 1 center who received adjunctive HBOT for necrotizing soft tissue infections with those in 30 patients at a different center who did not receive HBO. There was no significant difference in the mortality rate between the 2 groups; this was 4 of 48 (8%) in the HBOT group and 4 of 30 (13%) in the non-HBOT group (p=0.48). The median number of days in the intensive care unit and the median number of days in the hospital also did not differ significantly. There was a higher median number of débridement procedures per person in the HBOT group, 3.0 versus 2.0 in the non-HBOT group (p=0.03). Thus, based on the available evidence, HBOT for necrotizing soft tissue infections remains investigational.

**Refractory Mycoses**

No clinical trials on refractory mycoses (mucormycosis, actinomycosis, conidiobolus coronato) and cerebral edema were found. Therefore, these indications were changed to investigational.

**Acute Peripheral Arterial Insufficiency**

While Medicare has long listed acute peripheral arterial insufficiency as a medically necessary indication, this application was not addressed by previous versions of this policy. No clinical trial publications were identified that demonstrated benefit in HBOT for acute peripheral arterial insufficiency, and thus the evidence basis of the Medicare policy is unclear. Due to the lack of published literature, acute peripheral arterial insufficiency was added as an investigational indication in this policy.
Acute Coronary Syndromes

A 2011 Cochrane review by Bennett et al identified 6 trials with a total of 665 patients evaluating HBOT for acute coronary syndrome. All studies included patients with acute myocardial infarction (MI); 1 study also included individuals presenting with unstable angina. Additionally, all trials used HBOT as an adjunct to standard care. Control interventions varied; only 1 trial described using a sham therapy to blind participants to treatment group allocation. In a pooled analysis of data from 5 trials, there was a significantly lower rate of death in patients who received HBOT compared with a control intervention (RR=0.58; 95% CI: 0.36 to 0.92). Due to variability of outcome reporting in the studies, few other pooled analyses could be conducted. A pooled analysis of data from 3 trials on improvements in left ventricular function did not find a statistically significant benefit of HBOT (RR=0.09; 95% CI: 0.01 to 1.4). The authors noted that, although there is some evidence from small trials that HBO is associated with a lower risk of death, larger trials with high-quality methods are needed to determine which patients, if any, can be expected to derive benefit from HBO.

One of the trials was by Sharifi et al who randomly assigned 69 patients with unstable angina or MI to receive or not receive HBOT after a percutaneous coronary intervention (PCI). The 24 patients randomly assigned to the HBOT group reported only 1 adverse event (death, MI, coronary artery bypass, or revascularization of target lesion), compared with 13 in the 37 control patients. However, this study lacked adequate detail (e.g., on the type of PCI performed) to permit scientific conclusions. In another RCT of 64 patients, Alex et al concluded both neuropsychometric dysfunction and inflammatory response can be reduced postcardiopulmonary bypass when hyperbaric pretreatment is given. Based on this evidence, the treatment of acute coronary syndromes with HBOT is considered investigational.

Acute Ischemic Stroke

In a 2005 Cochrane systematic review, Bennett et al evaluated HBOT for acute stroke; the content of this review was updated in 2009. The investigators identified 6 RCTs with a total of 283 participants that compared HBOT with sham HBO or no treatment. The authors were only able to pool study findings for 1 outcome; the mortality rate at 3 to 6 months. A pooled analysis of data from 3 trials did not find a significant benefit of HBOT compared with a control condition for this outcome (RR=0.61; 95% CI: 0.17 to 2.20). One of the RCTs was published in 2003 by Rusyniak et al. This double-blind trial included 33 patients presenting with acute ischemic stroke who were randomly assigned to active or sham HBO. No beneficial effect was reported for HBOT compared with sham. Based on the available evidence, acute ischemic stroke is considered investigational.

Motor Dysfunction Associated with Stroke

In 2013, Efrati et al published an RCT evaluating HBOT for treatment of neurologic deficiencies associated with a history of stroke. The study included 74 patients with at least 1 motor dysfunction who had an ischemic or hemorrhagic stroke 6 to 36 months prior to study participation. Participants were randomly assigned to receive 2 months of HBOT (40 daily sessions, 5 d/wk, n=30) or delayed treatment (n=32). Patients were evaluated at baseline and 2 months. For patients in the delayed treatment control group, outcomes were evaluated at 4 months after crossing over and receiving HBOT. Twenty-nine of 32 patients (91%) in the delayed treatment group crossed over to the active intervention. Outcome measures included the National Institutes of Health Stroke Scale (NIHSS), which was measured by physicians blinded to treatment group, and several patient-reported quality-of-life and functional status measures.
At 2-month follow-up, there was statistically significantly greater improvement in function in the HBOT group than in the control group as measured by NIHSS, quality-of-life scales and the ability to perform activities of daily living (ADLs). These differences in outcome measures were accompanied by improvements in single photon emission computed tomography imaging in the regions affected by stroke. For the delayed treatment control group, there was a statistically significant improvement in function after HBOT compared with before treatment. This RCT raises the possibility that HBOT may induce improvements in function and quality of life for poststroke patients with motor deficits. However, the results are not definitive for a number of reasons. This RCT is small and enrolled a heterogeneous group of poststroke patients. The study was not double-blind and most outcome measures, except for NIHSS, were patient reported and thus prone to the placebo effect. Also, there was a high total dropout rate of 20% at the 2-month follow-up point. Therefore, larger, double-blind studies with longer follow-up are needed to corroborate these results. Because of these limitations in the evidence, HBOT is considered investigational for treating motor dysfunction associated with stroke.

**Bell Palsy**

In 2012, Holland et al published a Cochrane systematic review evaluating HBOT in adults with Bell palsy. The authors identified 1 RCT with 79 participants, and this study did not meet the Cochrane review's methodologic standards because the outcome assessor was not blinded to treatment allocation. Due to the publication of the Cochrane review and the finding of insufficient evidence, Bell palsy was added to the investigational statement.

**Traumatic Brain Injury**

A 2012 Cochrane systematic review addressed HBOT as adjunctive therapy for traumatic brain injury. The investigators identified 7 RCTs with a total of 571 participants comparing a standard intensive treatment regimen with the same treatment regimen plus HBO. The review did not include studies in which interventions occurred in a specialized acute care setting. The HBOT regimens varied among studies; for example, the total number of individual sessions varied from 3 to between 30 and 40. No trial used sham treatment or blinded the staff members who were treating the patients, and only 1 had blinding of outcome assessment. Allocation concealment was inadequate in all of the studies. The primary outcomes of the review were mortality and functional outcomes. A pooled analysis of data from 4 trials that reported this outcome found a statistically significantly greater reduction in mortality when HBOT was added to a standard treatment regimen (RR=0.69; 95% CI: 0.54 to 0.88). However, when data from the 4 trials were pooled, the difference in the proportion of patients with an unfavorable functional outcome at final follow-up was not statistically significant (RR=0.71; 95% CI: 0.50 to 1.01). Unfavorable outcome was commonly defined as a Glasgow Outcome Score of 1, 2, or 3, which are described as 'dead,' 'vegetative state,' or 'severely disabled.' Studies were generally small and were judged to have substantial risk of bias.

Several trials in military populations have been published. A sham-controlled double-blind trial evaluating HBOT was published by Wolf et al in 2012. The study included 50 military service members, 48 of whom were male, with combat-related mild traumatic brain injury. Participants were randomized to 30 sessions of HBOT over 8 weeks (n=25) or a sham intervention (room air at 1.3 atmosphere, absolute [ata]) (n=25). The primary outcome measures were scores on the Immediate Post-Concussive Assessment and Cognitive Testing (ImPACT) and Post-Traumatic Disorder Check List–Military Version (PCL-M) instruments. Patients were evaluated after every 5 treatment sessions and at 6 weeks postexposure. Forty-eight of 50 participants (96%) completed the study. There were no statistically significant differences on the ImPACT total mean score or the PCL-M
composite score at any time point. For example, at the 6-week follow-up, mean composite PCL-M scores were 41.6 in the HBOT group and 40.6 in the sham-control group (p=0.28). While the sample size was relatively small, the study was powered to detect clinically significant differences among groups on the cognitive tests.

In 2014, Cifu et al published findings of an RCT with 61 male Marines who had a history of mild traumatic brain injury and postconcussive syndrome. The study was sham-controlled and double-blinded. Patients were randomized to receive 1 of 3 treatments: 75% oxygen at 1.5 ata (n=21); 100% oxygen at 2.0 ata (n=19); and 3) sham treatment with normal air (n=21). Outcomes were assessed 3 months after the last exposure. The primary outcome was a clinically meaningful improvement, defined as a 10% difference between groups in the score on the Rivermead Post-Concussion Questionnaire (RPQ)-16 (scale ranges from 50 to 84, with higher values indicating more severe symptoms). At follow-up, there was no statistically significant difference among groups on RPQ-16 score (p=0.41). A variety of secondary outcomes were also assessed. None of these, including measures of attention, cognition, or depression, differed significantly among groups at follow-up.

In summary, systematic review of small trials with limitations found a mortality reduction with HBOT but no significant improvement in patient function among survivors of traumatic brain injury. Additional trials, conducted with military personnel, did not find significant benefits of HBOT in patients with mild traumatic brain injury. Thus, the evidence is insufficient that HBOT improves health outcomes in patients with traumatic brain injury, and this indication is considered investigational.

**Inflammatory Bowel Disease**

A 2014 systematic review by Dulai et al examined the evidence on HBOT for inflammatory bowel disease (Crohn's disease and ulcerative colitis). The review was not limited by study design. The authors included 17 studies: 1 RCT, 2 case-control studies, 3 case series, and 11 case reports. The studies reported on a total of 613 patients, 286 with Crohn’s disease and 327 with ulcerative colitis. The only RCT identified was published in 2013; it was open-label and included 18 patients with ulcerative colitis. Patients were randomized to treatment with standard medical therapy only (n=8) or medical therapy plus HBOT (n=10). The hyperbaric oxygen intervention consisted of 90 minutes of treatment at 2.4 atm, 5 days a week for 6 weeks (total of 30 sessions). The primary outcome was the Mayo score, which has a potential range of 0 to 12. Patients with a score of 6 or more are considered to have moderate to severe active disease. At follow-up, there was no significant difference between groups in the Mayo score; the median score at 6 months was 0.5 in the HBOT group and 3 in the control group (exact p value not reported). In addition, there were no significant differences in any of the secondary outcomes, including laboratory tests and fecal weight. This is a small study that may have been underpowered. Overall, the authors found that the studies had a high risk of bias, particularly in the areas of attrition and reporting bias.

In summary, there is insufficient evidence that HBOT is effective for treating inflammatory bowel disease. Only 1 small RCT has been published, and this study did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy.

**Idiopathic Sudden Sensorineural Hearing Loss**

In 2011, UHMS added idiopathic sudden sensorineural hearing loss (ISSNHL) within the past 14 days as an approved indication for HBOT.
A 2012 Cochrane review on HBOT for ISSNHL and tinnitus identified 7 RCTs with a total of 392 participants. All trials included patients with ISSNHL with and/or without tinnitus; 2 trials also included patients with tinnitus in the absence of ISSNHL. Randomization procedures were only described in 1 study, and only 1 study stated they blinded participants to treatment group assignment using sham therapy. Six of the studies included time-based entry criteria for hearing loss and/or tinnitus; this was 48 hours in 3 studies, 2 weeks in 2 studies (for acute presentation), and 6 months in 1 study. The dose of oxygen per treatment session and the treatment protocols varied among studies, e.g., the total number of treatment sessions varied from 10 to 25.

All trials reported on change in hearing following treatment; but specific outcomes varied. Two trials reported the proportion of participants with greater than 50% return of hearing at the end of therapy. A pooled analysis of these studies did not find a statistically significant difference in outcomes between the HBOT and the control groups (RR=1.53; 95% CI: 0.86 to 2.78). In contrast, a pooled analysis of 2 trials reporting the proportion of participants with greater than 25% return of hearing at the end of therapy found a significantly higher rate of improvement after HBOT than a control intervention (RR=1.39; 95% CI: 1.05 to 1.84). Moreover, a pooled analysis of 4 trials found a significantly greater mean improvement in hearing over all frequencies with HBOT compared with control (mean difference, 15.6 dB; 95% CI: 1.5 to 29.8). The authors stated that, due to methodologic shortcomings of the trials and the modest number of patients, results of the meta-analysis should be interpreted cautiously; they did not recommend use of HBOT for treating ISSNHL.

In 2013, Cvorovic et al published an RCT that included 50 patients with ISSNHL who had failed primary therapy with intravenous steroids. Patients were randomized to receive HBOT (20 sessions, 5 daily sessions per week) or intratympanic steroid injection (4 injections in 13 days). The HBOT sessions consisted of 10 minutes of compression on air, 60 minutes of 100% oxygen at 2 ata, and 10 minutes of decompression on air. Outcomes were change in the mean hearing thresholds at each of 5 frequencies (0.25, 0.5, 1, 2, and 4 kHz). After treatment, there were no statistically significant differences in mean hearing thresholds at 4 of the 5 frequencies. The exception was 2 kHz, and at this frequency, the improvement was significantly greater in the HBOT group.

Due to methodologic limitations and variability among published studies, as well as inconsistent findings, the evidence is insufficient to draw conclusions about the effect of HBOT on health outcomes in patients with ISSNHL. Thus, HBOT is considered investigational for treating ISSNHL.

Cancer Treatment

In an RCT of 32 patients, Heys et al found no increase in 5-year survival in patients treated with HBOT prior to chemotherapy for locally advanced breast carcinoma to increase tumor vascularity. This approach is being studied because studies in animal models have suggested that HBOT increases tumor vascularity and thus may make chemotherapy more effective. In a Cochrane review, Bennett et al concluded that HBOT given with radiotherapy may be useful in tumor control; however, the authors expressed caution because significant adverse effects were common with HBOT and indicated further study would be useful. Therefore, a policy statement was added to indicate HBOT for tumor sensitization for cancer treatments, including but not limited to radiotherapy or chemotherapy, is considered investigational.

In Vitro Fertilization

Van Voorhis et al reported that HBOT was well-tolerated in women undergoing ovarian follicular stimulation for in vitro fertilization; however, no outcomes were reported, and
further study is needed. In vitro fertilization was added to the list of investigational indications for HBO.

**Delayed-Onset Muscle Soreness**

In a Cochrane review, Bennett et al concluded that available evidence is insufficient to demonstrate beneficial outcomes with HBOT for delayed-onset muscle soreness and closed soft tissue injury. It was noted that HBOT possibly increases pain initially and further studies are needed. Therefore, a policy statement was added to indicate HBOT for delayed-onset muscle soreness is considered investigational.

**Autism Spectrum Disorders**

A 2012 systematic review of evidence on HBOT for treatment of children with autism identified 2 RCTs with a total of 89 participants. One of the 2 RCTs found better outcomes after HBOT compared with placebo treatment, and the other did not find significant differences in outcomes. The author concluded that additional sham-controlled trials with rigorous methodology are needed to draw conclusions about the efficacy of HBOT for treating autism. A 2012 review article also concluded that, although studies to date suggest that HBOT is safe and potentially effective, additional studies are warranted. In particular, it was recommended that future studies use standardized behavioral measurement tools and also assess physiologic biomarkers.

One of the RCTs was by Rossignol et al. This double-blind trial included 62 children, ages 2 to 7 years, who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for autistic disorder. The active treatment was hyperbaric treatment at 1.3 atm and 24% oxygen in a hyperbaric chamber. (This regimen differs from standard HBOT, which uses 100% oxygen and a pressure of at least 1.4 atm.) The other group received a sham treatment consisting of 1.03 atm and ambient air (21% oxygen). Both groups received 40 sessions of active or sham treatment lasting 60 minutes each over 4 weeks. The equipment, procedures, etc. in the 2 groups were as similar as possible to maintain blinding. The investigators, participants, parents, and clinic staff were blinded to treatment group. Only the hyperbaric technician, who had no role in outcome assessment, was aware of group assignment. After completion of the 4-week study, families with children in the control group were offered the active intervention. When asked at the end of the study, there was no significant difference in the ability of parents to correctly guess the group assignment of their child.

The outcomes were change versus baseline after 4 weeks on the following scales: Aberrant Behavior Checklist (ABC) total score and 5 subscales; Autism Treatment Evaluation Checklist (ATEC) total score and 4 subscales; and Clinical Global Impression—Improvement (CGI) overall functioning score and 18 subscales. P values of less than 0.05 were considered statistically significant; there was no adjustment for multiple comparisons. The analysis included all children who completed at least 1 complete session. Of the 33 children assigned to active treatment, 30 were included in the analysis, and 29 completed all 40 treatments. Of the 29 children assigned to the control treatment, 26 completed all 40 sessions and were included in the analysis.

There was no significant between-group improvement on the ABC total score, any of the ABC subscales, or on the ATEC total score. Compared with the control group, the treatment group had a significant improvement in 1 of 4 subscales of the ATEC, the Sensory/Cognitive Awareness subscale. The change from baseline on this subscale was a mean of 16.5 in the treatment group and a mean of 5.4 in the control group, a difference of 11.1 (p=0.037). (Note: due to an administrative error, baseline ATEC was not collected at 1 site, and thus data were not available for 23 children in the treatment group and 21 children in the control group.) On the physician-rated CGI total score, 9 of
30 (30%) children in the treatment group had a score of 1 (very much improved) or 2 (much improved) compared with 2 of 26 (8%) in the control group (p=0.047). On the parental-rated CGI total score, 9 of 30 (30%) children in the treatment group had a score of 1 or 2 compared with 4 of 26 (15%) in the control group (p=0.22, not statistically significant). (The exact numbers receiving scores of 1 vs. 2 were not reported.) Change in mean CGI scores was also reported, but this may be a less appropriate way to analyze these data. Among the parental-rated CGI subscales, significantly more children were rated as improved in the treatment group compared with controls on 2 of 18 subscales, Receptive Language (p=0.017) and Eye Contact (p=0.032).

A key limitation of this study was that the authors reported only outcomes at 4 weeks, directly after completion of the intervention. It is not known whether there were any long-term effects. Additional follow-up data cannot be obtained because members of the control group crossed over to the intervention after 4 weeks. Other limitations include lack of adjustment for multiple comparisons and unclear clinical significance of the statistically significant outcomes. UHMS issued a position paper after publication of the Rossignol et al study stating that it still did not recommend routine HBOT for autism.57

An additional 2012 RCT, published after the 2012 systematic review had been completed, was conducted in Thailand and randomly assigned 60 children with autism to receive 20 one-hour sessions with HBOT or sham air (n=30 per group).58 The primary outcome measures were change in ATEC and CGI scores, evaluated separately by clinicians and parents. There were no statistically significant differences between groups for any of the primary outcomes. For example, post-treatment clinician-assessed mean scores on ATEC were 52.4 in the HBOT group and 52.9 in the sham air group. In summary, there is insufficient evidence from rigorous RCTs that HBOT improves health outcomes for patients with autism spectrum disorder; therefore, HBOT for this indication is considered investigational.

**Amyotrophic Lateral Sclerosis**

In the updated searches, no randomized trials were found evaluating HBOT for treatment of amyotrophic lateral sclerosis. In a small case series, Steele et al treated 5 patients with HBOT and reported some improvements in fatigue but noted that further study is needed, and attention to placebo effects must be given.59 Thus, amyotrophic lateral sclerosis was added to the policy as an investigational indication.

**Cerebral Palsy**

Two published RCTs were identified. In 2012, Lacey et al published a double-blind RCT that included 49 children age 3 to 8 years with spastic cerebral palsy.60 Participants were randomized to receive 40 treatments with either HBOT (n=25) or hyperbaric air to simulate 21% oxygen at room air (n=24). The primary efficacy outcome was change in the Gross Motor Function Measure (GMFM-88) global score after the 8-week treatment period. The study was stopped early due to futility, when an interim analysis indicated that there was less than a 2% likelihood that a statistically significant difference between groups would be found. At the time of the interim analysis, the posttreatment GMFM-88 global score was a mean (SD) of 40.8 (33.4) in the HBOT group and 41.2 (29.6) in the hyperbaric air group. The between-group difference was 0.9 (95% CI: -1.5 to 3.3; p=0.54).

Previously, in 2001, Collet et al randomly assigned 111 children with cerebral palsy to 40 treatments over a 2-month period of either HBOT (n=57) or slightly pressurized room air (n=54).61 The authors found HBOT produced similar improvements in outcomes such as gross motor function and ADLs in both groups as slightly pressurized air. The available evidence does not support HBOT for cerebral palsy; therefore, this is considered investigational.
Vascular Dementia

A 2012 Cochrane review identified 1 RCT evaluating HBOT for vascular dementia. The 2009 study, conducted in China compared HBO plus donepezil to donepezil-only in 64 patients. The HBOT plus donepezil group had significantly better cognitive function after 12 weeks of treatment, as assessed by the Mini-Mental State Examination. The Cochrane investigators judged the trial to be of poor quality because it was not blinded and the methods of randomization and allocation concealment were not discussed. This single trial with limitations provides insufficient evidence on the efficacy of HBOT on vascular dementia; thus, HBOT is considered investigational for this indication.

Radiotherapy Adverse Effects

In 2010, Spiegelberg et al conducted a systematic review of studies on HBOT to prevent or treat radiotherapy-induced head and neck injuries associated with treatment of malignant tumors. The authors identified 20 studies. Eight of the studies included control groups; their sample sizes ranged from 19 to 78 subjects. Four (50%) of the studies with a control group concluded that HBOT was effective, and the other 4 did not. The authors noted a paucity of RCTs but did not state the number of RCTs that they identified in their review.

A study by Teguh et al published in 2009 included 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiotherapy; the study was conducted in The Netherlands. HBOT was used to prevent adverse events following radiotherapy. Eight patients were randomly assigned to receive 30 sessions of HBO, beginning within 2 days of completing radiotherapy, and 9 patients received no additional treatment. All patients were included in the analysis. Quality-of-life outcomes were assessed, and the primary outcome was specified as xerostomia at 1 year. Quality-of-life measures did not differ significantly between groups in the acute phase (first 3 months). For example, 1 month after treatment, the mean visual analog scale (VAS) score for xerostomia (0-to-10 scale) was 5 in the HBOT group and 6 in the control group. However, at 1 year, there was a statistically significant difference between groups; the mean VAS score for xerostomia was 4 in the HBOT group and 7 in the control group (p=0.002). Also at 1 year, the mean quality-of-life score for swallowing (0-to-100 scale) was 7 in the HBOT group and 40 in the control group (p<0.001). The study is limited by the small sample size and the wide fluctuation over the follow-up period in quality-of-life ratings.

In 2010, Gothard et al in the U.K. published findings of an RCT using HBOT for arm lymphedema occurring after radiotherapy for cancer. Fifty-eight patients with arm lymphedema (at least 15% increase in arm volume) following cancer treatment were randomized in a 2:1 ratio to receive HBOT (n=38) or usual care without HBOT (n=20). Fifty-three patients had baseline assessments and 46 of 58 (79%) had 12-month assessments. At the 12-month follow-up, there was no statistically significant difference in the change from baseline in arm volume. The median change from baseline was -2.9% in the treatment group and -0.3% in the control group. The study protocol defined response as at least an 8% reduction in arm volume relative to the contralateral arm. According to this definition, 9 of 30 (30%) of patients in the HBOT group were considered responders compared with 3 of 16 (19%) in the control group; the difference between groups was not statistically significant. Other outcomes, e.g., quality-of-life scores on the 36-Item Short-Form Health Survey, were similar between groups.

Due to the limited data, use of HBOT in patients with arm lymphedema or radiation-induced injury in the head and neck after radiotherapy, as well as early use of HBOT after radiotherapy to reduce adverse effects, are considered investigational.
**Idiopathic Femoral Neck Necrosis**

A double-blind RCT that evaluated HBOT to treat femoral head necrosis was published in 2010 by Camporesi et al.66 The study included 20 adult patients with idiopathic unilateral femoral head necrosis. Patients received 30 treatments over 6 weeks with either HBOT at 2.5 ata (n=10) or a sham treatment consisting of hyperbaric air (n=10). The mean severity of pain on a 0-to-10 scale was significantly lower in the HBOT group than the control group after 30 sessions (p<0.001) but not after 10 or 20 sessions. (The article did not report exact pain scores.) Several range-of-motion outcomes were also reported. At the end of the initial treatment period, extension, abduction, and adduction, but not flexion, were significantly greater in the HBOT group than in the control group. Longer term comparative data were not available because the control group was offered HBOT at the end of the initial 6-week treatment period. This single, small short-term RCT represents insufficient data on which to draw conclusions about the efficacy of HBOT for femoral head necrosis.

**Migraine**

A 2008 Cochrane review by Bennett et al identified RCTs that evaluated the effectiveness of systemic HBOT for preventing or treating migraine headache compared with another treatment or a sham control.67 In a search of the literature through May 2008, 5 trials with a total of 103 patients were identified that addressed treatment of acute migraine with HBO. A pooled analysis of 3 trials (total of 43 patients) found a statistically significant increase in the proportion of patients with substantial relief of migraine within 45 minutes of HBOT (RR=5.97; 95% CI: 1.46 to 24.38; p=0.001). No other pooled analyses were conducted due to variability in the outcomes reported in the trials. The meta-analysis does not report data on treatment effectiveness beyond the immediate post-treatment period, and the quality of trials' methodology was moderate to low, e.g., randomization was not well-described in any trial. Based on the above limitations of the meta-analysis, use of HBOT for migraine remains investigational.

**Herpes Zoster**

In 2012, Peng et al in China published an RCT evaluating HBOT for herpes zoster.68 Sixty-eight patients with herpes zoster diagnosed within the previous 2 weeks were randomized to 30 sessions of HBOT (n=36) or medication treatment (n=32). Pharmacotherapy included antiviral, pain, nerve nutritive, and antidepressive medication. Therapeutic efficacy was calculated at the end of the 3-week treatment period and included the proportion of patients who were healed (i.e., complete subsidence of pain and rash) or improved (i.e., significant pain relief and rash subsistence). Rates of therapeutic efficacy were 97.2% in the HBOT group and 81.3% in the medication group. The difference between groups was statistically significant (p<0.05). In the HBOT group, 22 of 36 patients (61%) were considered to be healed and 13 (36%) were improved. In the medication group, 17 of 32 (53%) patients were healed and 9 (28%) were improved. Limitations of the study included a lack of blinding and lack of long-term follow-up. The evidence from this single RCT is insufficient to draw conclusions about the effect of HBOT on health outcomes for patients with herpes zoster; therefore, HBOT is considered investigational for this indication.

**Ongoing and Unpublished Clinical Trials**

No relevant trials were identified.
Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

In response to requests, input was received through 6 physician specialty societies and 5 academic medical centers while this policy was under review in 2010. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. The clinical input varied depending on the condition. There was universal agreement that topical hyperbaric therapy and systemic HBOT for autism spectrum disorders and headache/migraine are investigational. There was also wide support for changing acute carbon monoxide poisoning, compromised skin grafts or flaps, chronic refractory osteomyelitis, and necrotizing soft tissue infections to the list of medically necessary indications for HBOT. Several reviewers acknowledged that there is a paucity of clinical trials on HBOT for compromised skin grafts/flaps, necrotizing soft tissue infections, and chronic refractory osteomyelitis. These reviewers commented on the support from basic science, animal studies, and retrospective case series, as well as lack of effective alternative treatments for these conditions. Based on the available evidence and clinical input, acute carbon monoxide poisoning and chronic refractory osteomyelitis were changed in 2010 to medically necessary indications for HBOT. However, despite the clinical input and given the limited published evidence, compromised skin grafts and flaps and necrotizing soft tissue infections are still considered investigational.

Summary of Evidence

Based on reviews of the medical literature and clinical input, systemic hyperbaric oxygen therapy (HBOT) may be considered medically necessary for selected indications (specified in the Policy section) and investigational for all other indications. Topical HBOT is considered investigational.

Supplemental Information

Practice Guidelines and Position Statements

In 2011, the Undersea and Hyperbaric Medical Society (UHMS) updated their list of indications considered appropriate for HBOT. These indications are as follows:

- Air or gas embolism
- Carbon monoxide poisoning and carbon monoxide complicated by cyanide poisoning
- Clostridial myositis and myonecrosis (gas gangrene)
- Crush injury, compartment syndrome, and other acute traumatic ischemias
- Decompression sickness
- Arterial insufficiencies
  - Central retinal artery occlusion
  - Enhancement of healing in selected problem wounds
- Severe anemia
- Intracranial abscess
- Necrotizing soft tissue infections
• Osteomyelitis (refractory)
• Delayed radiation injury (soft tissue and bony necrosis)
• Skin grafts and flaps (compromised)
• Acute thermal burn injury
• Idiopathic sudden sensorineural hearing loss (ISSNHL) (patients with moderate to profound ISSNHL who present within 14 days of symptom onset)

In 2012, the American Academy of Otolaryngology-Head and Neck Surgery published a clinical guideline on treatment of sudden hearing loss. The guideline includes a statement that HBO may be considered a treatment option for patients who present within 3 months of a diagnosis of ISSNHL. The document states, “Although HBO is not widely available in the United States and is not recognized by many U.S. clinicians as an intervention for ISSNHL, the panel felt that the level of evidence for hearing improvement, albeit modest and imprecise, was sufficient to promote greater awareness of HBO as an intervention for [this condition].”

**U.S. Preventive Services Task Force Recommendations**

HBOT is not a preventive service.

**Medicare National Coverage**

As of April 1, 2003, the Centers for Medicare and Medicaid added Medicare coverage of HBO for diabetic wounds of the lower extremities meeting certain criteria. Medicare coverage is provided for HBO administered in a chamber for the following conditions:

• Acute carbon monoxide intoxication (ICD-9-CM diagnosis 986)
• Decompression illness (ICD-9-CM diagnosis 993.2, 993.3)
• Gas embolism (ICD-9-CM diagnosis 958.0, 999.1)
• Gas gangrene (ICD-9-CM diagnosis 0400)
• Acute traumatic peripheral ischemia. HBO is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened (ICD-9-CM diagnosis 902.53, 903.01, 903.1, 904.0, 904.41).
• Crush injuries and suturing of severed limbs. As in the previous conditions, HBO would be an adjunctive treatment when loss of function, limb, or life is threatened (ICD-9-CM diagnosis 927.00-927.03, 927.09-927.11, 927.20-927.21, 927.8-927.9, 928.00-928.01, 928.10-928.11, 928.20-928.21, 928.3, 928.8-928.9, 929.0, 929.9, 996.90-996.99).
• Progressive necrotizing infections (necrotizing fasciitis) (ICD-9-CM diagnosis 728.86)
• Acute peripheral arterial insufficiency (ICD-9-CM diagnosis 444.21, 444.22, 81)
• Preparation and preservation of compromised skin grafts (not for primary management of wounds) (ICD-9-CM diagnosis 996.52; excludes artificial skin graft)
• Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management (ICD-9-CM diagnosis 730.10-730.19)
• Osteoradionecrosis as an adjunct to conventional treatment (ICD-9-CM diagnosis 526.89)
• Soft tissue radionecrosis as an adjunct to conventional treatment (ICD-9-CM diagnosis 990)
• Cyanide poisoning (ICD-9-CM diagnosis 987.7, 989.0)
• Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment (ICD-9-CM diagnosis 039.0-039.4, 039.8, 039.9)
• Diabetic wounds of the lower extremities in patients who meet the following 3 criteria:
  o Patient has type I or type II diabetes and has a lower extremity wound that is a result of diabetes;
  o Patient has a wound classified as Wagner grade III or higher; and
  o Patient has failed an adequate course of standard wound therapy.

The use of HBOT is covered as adjunctive therapy only after there are no measurable signs of healing for at least 30 days of treatment with standard wound therapy and must be used in addition to standard wound care. Standard wound care in patients with diabetic wounds includes: assessment of a patient’s vascular status and correction of any vascular problems in the affected limb, if possible, optimization of nutritional status, optimization of glucose control, débridement by any means to remove devitalized tissue, maintenance of a clean, moist bed of granulation tissue with appropriate moist dressings, appropriate off-loading, and necessary treatment to resolve any infection that might be present. Failure to respond to standard wound care occurs when there are no measurable signs of healing for at least 30 consecutive days. Wounds must be evaluated at least every 30 days during administration of HBOT. Continued treatment with HBOT is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.

Medicare continues to consider topical HBOT ineligible for coverage.

Note: Medicare differs from BCBS policy in that it provides coverage for systemic HBOT for acute carbon monoxide intoxication, actinomycosis, acute peripheral arterial insufficiency, compromised skin grafts or flaps, chronic refractory osteomyelitis, and necrotizing soft tissue infections. However, as noted here, literature searches did not reveal sufficient evidence to consider these appropriate indications for HBOT.

References

7. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Hyperbaric oxygen therapy for wound healing- part II. TEC Assessments 1999;Volume 14, Tab 15. PMID
8. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Hyperbaric oxygen therapy for wound healing- part III. TEC Assessments 1999;Volume 14, Tab 16. PMID


**Documentation Required for Clinical Review**

- History and physical and/or consultation report including:
  - Diagnosis substantiating hyperbaric oxygen therapy
  - Previous treatment and response
- Proposed treatment plan (including number of treatment sessions) or progress notes of ongoing treatment
- Operative report(s)
• Wound description (if applicable) including:
  o Wound location, size, and description of wound bed
  o Wagner wound classification
  o Wound therapy treatments over the last 30 days
  o Wound progress

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

MN/IE

The following service/procedure may be considered medically necessary in certain instances and investigational in others. Services may be medically necessary when policy criteria are met. Services are considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

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<tr>
<th>Type</th>
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<th>Description</th>
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<td>CPT®</td>
<td>99183</td>
<td>Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session</td>
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<td>HCPC</td>
<td>G0277</td>
<td>Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval</td>
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<tr>
<td></td>
<td>A4575</td>
<td>Topical hyperbaric oxygen chamber, disposable</td>
</tr>
<tr>
<td></td>
<td>E0446</td>
<td>Topical oxygen delivery system, not otherwise specified, includes all supplies and accessories</td>
</tr>
<tr>
<td>ICD-9 Procedure</td>
<td>93.95</td>
<td>Hyperbaric oxygenation</td>
</tr>
<tr>
<td></td>
<td>93.59</td>
<td>Other immobilization, pressure, and attention to wound</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Procedure</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>For dates of service on or after 10/01/2015</td>
<td>6A150ZZ, 6A151ZZ</td>
<td>Extracorporeal therapies, decompression, circulatory - single and multiple duration codes (used for decompression sickness treatment)</td>
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<tr>
<td></td>
<td>5A05121, 5A05221</td>
<td>Extracorporeal assistance and performance, circulatory, oxygenation, hyperbaric - intermittent and continuous codes</td>
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</table>

<table>
<thead>
<tr>
<th>ICD-9 Diagnosis</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Diagnoses</td>
<td></td>
<td>All Diagnoses</td>
</tr>
</tbody>
</table>
Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/16/1984</td>
<td>New Policy Adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>10/11/1995</td>
<td>Policy Revision</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>6/7/2000</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>8/1/2002</td>
<td>Administrative Review</td>
<td>Administrative Review</td>
</tr>
<tr>
<td>12/1/2006</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>12/10/2008</td>
<td>Policy Revision</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>7/2/2010</td>
<td>Policy revision with position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>1/21/2011</td>
<td>Coding Update</td>
<td>Administrative Review</td>
</tr>
<tr>
<td>9/27/2013</td>
<td>Policy revision with position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>5/2/2014</td>
<td>Policy title change from Hyperbaric Oxygen Therapy (HBOT) Policy revision with position change effective July 11, 2014</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>1/30/2015</td>
<td>Policy revision without position change</td>
<td>Coding Update</td>
</tr>
</tbody>
</table>

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements

This service (or procedure) is considered medically necessary in certain instances and investigational in others (refer to policy for details).
For instances when the indication is **medically necessary**, clinical evidence is required to determine medical necessity.

For instances when the indication is **investigational**, you may submit additional information to the Prior Authorization Department.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal [www.blueshieldca.com/provider](http://www.blueshieldca.com/provider).

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.