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Overview

This Coverage Policy addresses the use of cold therapy units, cooling devices, cooling garments and scalp cooling for prevention of chemotherapy-induced alopecia.

Coverage Policy

Coverage for cryounits and cryotherapy machines varies across plans. Refer to the customer’s benefit plan document for coverage details. When covered, coverage for cryounits and cryotherapy machines is subject to the terms, conditions and limitations of the applicable benefit plan’s Durable Medical Equipment (DME) benefit and schedule of copayments.

A cold therapy unit or cooling device (HCPCS codes E0218, E0236), including both passive and active pump-controlled cooling and compression devices (HCPCS code E1399), for any indication is considered a convenience item and not medically necessary.

A cooling device/cooling garment (HCPCS code E1399) for the treatment of multiple sclerosis is considered experimental, investigational or unproven.

Scalp cooling for prevention of chemotherapy-induced alopecia is considered not medically necessary.
General Background

Cryotherapy, or cold therapy, is the therapeutic application of cold. It is a widely used modality in the field of physical medicine and rehabilitation, and is often used in conjunction with other rehabilitation treatments to reduce inflammation and relieve pain. Cold therapy has a long history of being used as a standard treatment for soft tissue injury. It is also frequently used as part of postoperative rehabilitation after orthopedic surgery, in particular, knee surgery. The exact mechanism by which cold therapy works is not completely known or understood. It is thought that this modality causes a decrease in temperature, resulting in a reduction of the metabolic rate, thereby decreasing inflammation, edema, muscle spasm and pain. It has also been noted that, after the initial vasoconstriction, there may be an increase in skin blood flow after local ice application, causing a reflex vasodilation. Multiple variables, including room temperature, temperature of ice or cooling agent, thickness of subcutaneous fat, thickness of dressings, method of application, and duration of application, appear to have bearing on the effect of cold therapy.

Cold therapy can be administered using several methods. These include cold immersion, ice massage, application of ice/crushed ice, and use of a gel ice pack, instant ice packs, vapocoolant spray or cooling devices. Compression therapy is generally provided postoperative with compressive wraps such as an Ace bandage or wrap.

Application of ice is often combined with compression and elevation in clinical trials, making it difficult to evaluate the efficacy of this treatment as the sole modality. Few clinical trials have been undertaken to assess the effect of this modality alone in the treatment of specific medical conditions. The mode, frequency, and duration of the ice application vary widely across studies. As with many other rehabilitation interventions, the therapeutic application of cold is based largely on empirical experience.

Cooling Devices

Cooling devices may also be referred to as cold therapy units, cryounits, or cryotherapy machines. Cooling devices may be passive or active and operate by gravity or the use of a mechanical or pneumatic pump. The intended purpose of these devices is to provide a combination of cooling and compression to treat musculoskeletal conditions.

Passive cold therapy devices operate by gravity or a hand pump with no battery or electricity used. Generally they consist of a cuff or wrap and a cooler. Ice water is placed in the reservoir or cooler. The cooler is placed above the body area or joint and then utilizes gravity to fill the cuff and compress the joint. If a hand pump is used the device may be placed closer to or level with the joint or area being treated.

Active cooling devices include pneumatic or mechanical pumps that may be battery or electric operated. The intended function of the pump is to provide cyclical compression and cooling to the affected area. The purpose of the compression is to remove fluid and decrease edema while providing the cooling. The devices generally consist of two basic parts: a wrap or wrap system that is designed to cover specific areas of the body; and a control unit, which is filled with ice and water. The control unit or pump circulates the cooled water through the wraps to the affected area. The devices may also contain a cooler or refrigeration component. Some of these devices are also designed to provide heat therapy.

Available passive or gravity-controlled cold therapy devices that provide cooling and compression include, but are not limited to:

- ArcticFlow Cold therapy system (dj Orthopedics, Inc., Vista, CA): This device has a gravity-controlled system.
- Cryo/Cuff™ (Aircast®, Summit, NJ): This device has a gravity-controlled system.
- EBI® Gravity Cold Therapy System (Biomet, Inc., Parsippany, NJ): This device has a gravity-driven format.
- Polar Care Cub (BREG, Inc., McKinney, TX): This device includes a pad and hand pump that is used to circulate the water.
Available active cold therapy devices that operate by battery or electric powered pump that provide cooling and compression include, but are not limited to:

- AutoChill® system (Aircast®, Summit, NJ): This device is an accessory to the CryoCuff® system that utilizes an electronic pump in order to continuously cycle water between cooler and cuff.
- BioCryo Cold Compression System (Bio Compression Systems, Inc., Moonachie, New Jersey): This device includes a gradient, sequential, pneumatic compression pump.
- Cryotherapy Cold Water Therapy System by Artic® Ice (Healio Health, Akron, OH): This device includes electric pump and pad.
- DeRoyal® Cold Therapy Unit (DeRoyal Industries, Powell, TN): Includes pump motor that circulates water between unit bucket and cooling blanket.
- EBIce® Cold Therapy System (Biomet, Inc., Parsippany, NJ): Intermittent pump cycle with adjustable treatment setting controls water temperature and intermittent massage.
- Game Ready™ Accelerated Recovery System (CoolSystems, Inc., Berkeley, CA): This device contains an electric or battery-run pump.
- Iceman Cold Therapy unit (DJO Incorporated Inc., Vista, CA): This device includes pad and electric pump to circulate the fluid.
- Nanotherm™ (ThermoTek, Carrollton, TX): This devices includes pneumatic pump and provides heating, cooling and compression therapies.
- OPTI-ICE™ Cold Therapy System (Chattanooga Group, Hixson, TN): This device includes an electric pump.
- Polar Care 500, Polar Care 300 (BREG, Inc., McKinney, TX): This device includes a pad and battery/electric pump that is used to circulate the water.
- TEC Iceless Cold Therapy/Compression/DVT Prophylaxis (Maldonado Medical LLC, Phoenix, Arizona): this product provides iceless cold therapy/compression/ deep vein thrombosis (DVT) DVT prophylaxis
- VitalWrap System® (VitalWear Inc., South San Francisco, CA): This device provides heating, cooling, and compression therapies. The device includes a control unit, tubing set, and a thermal fabric wrap. The control unit, which includes a fluid reservoir, manages the temperature of water used by the system to supply heat or cold to the fabric wrap that is attached to the body.
- Vascutherm™ (ThermoTek, Carrollton, TX): Includes pneumatic pump and provides heating, cooling and compression therapies. The device also includes a deep vein thrombosis (DVT) mode—this is a compression (or air)-only mode, that is intended to prevent DVT.

Cooling Garments for Multiple Sclerosis

Multiple sclerosis (MS) is a chronic, progressive, neurologic autoimmune disorder that affects the myelin sheath surrounding the axons in the central nervous system (CNS). The symptoms may be mild or severe, of long or short duration, and appear in different combinations depending on the area of the nervous system that is involved (National Institute of Neurological Disorders and Stroke [NINDS], 2015). The disease course is largely unpredictable. The disease can result in a wide array of symptoms including: muscle weakness, spasticity, impairment of pain, temperature and touch senses, pain (moderate to severe), ataxia, tremor, speech disturbances, vision disturbances, vertigo, bowel, bladder, sexual dysfunction, depression, cognitive abnormalities, and fatigue (NINDS, 2015). Treatment of MS is related to the course of the disease and symptoms that are experienced. The goals of treatment are to improve recovery from attacks; to prevent or lessen the number of relapses; and to halt the disease progression.

It has been reported in the medical literature that heat, whether generated by temperatures outside the body or by exercise, causes temporary worsening of many MS-related symptoms in many patients (NINDS, 2015). In particular, it has been noted that the symptom of fatigue may increase with an elevated body temperature. Fatigue has been noted to be a common and debilitating symptom of MS, affecting many patients (Shapiro, 2005). Various interventions have been proposed for treatment of fatigue, including medication, aerobic exercise, adequate rest, cooling systems and alternative therapies. Various cooling devices or cooling garments have been developed to treat heat sensitivity in a patient with MS. These devices are also used for a variety of industrial, military and recreational applications.
Active Cooling Devices: Active cooling devices, also known as cooling suits or liquid-cooled garments, have separate mechanisms (e.g., pumps) that attach to the garments, circulating coolant through tubes in the garments.

Available active cooling devices and garments include, but are not limited to:

- FAST® Personal Medical Cooling Suit System (Fast Race Products, Mount Prospect, IL): This device includes a t-shirt, cooler, pump system and hoses.
- Polar Active Cooling Vest (Polar Products Inc., Akron, OH)

Passive Cooling Devices: Passive cooling refers to cooling with no active mechanism such as a separate pump. This type of device is usually a garment such as a vest or collar that works by placing ice or gel packs into the pockets of a vest or by placing the garment in a freezer to pre-cool it. Many of these devices were developed for other uses in industry and recreation to combat heat and are now also marketed for medical purposes.

Available passive cooling garments include but are not limited to:

- Cooltemp Vest (Life Enhancement Technologies, Inc., Santa Clara, CA): This garment consists of a vest with four pockets for ice insertion.
- SteeleVest® Body Cooling Comfort System™ (Kingston, WA): This vest includes frozen Thermo-strips (starch-based gel ice packs that can be frozen in a household freezer) that are inserted into the insulated SteeleVest.
- HeatShield™ (SummitStone Corporation, White Stone, VA): This garment consists of a vest that is placed in the freezer overnight.
- Chill-Its® cooling vests, hats, headbands (Ergodyne, St. Paul, MN): These are evaporative cooling garments that are chilled in the freezer before use.

Scalp Cooling for Chemotherapy-Induced Alopecia

Scalp cooling has been proposed to prevent chemotherapy-induced alopecia (CIA). Scalp cooling devices and caps are intended to reduce the likelihood of CIA by inducing vasoconstriction, thereby reducing the local uptake of chemotherapy agent, the metabolic rate of the hair follicle, or both. It is hypothesized that the cold treatment provides protection through the cutaneous vasoconstriction of the scalp vasculature. Reduced blood flow to the scalp may decrease the concentration of chemotherapy that the scalp is exposed to, decrease the cellular uptake of chemotherapy by the hair follicle, and/or reduce the metabolic rate of the hair follicle. The devices are available either as non-automated, ice-filled cooling caps that require changing during treatment because of thawing, or automated systems connected to cooling caps that continuously circulate cooling solution to maintain the proper scalp temperature (Hayes, 2018).

Commercially available precooled nonautomated caps include Penguin Cold Caps (Penguin Cold Caps and Chemo Cold Caps (Chemotherapy Cold Caps Inc.). These older technologies can be heavy to wear, require replacement approximately 2 to 3 times per treatment session due to thawing, and have been associated with cold thermal burns (e.g., frostbite) (Shah et al., 2018). These caps are not subject to Food and Drug Administration (FDA) regulation or prescription, and patients may rent them directly from the manufacturers. Newer technologies for scalp cooling systems are self-contained, with built-in temperature sensors that cool and circulate a glycol-based fluid through channels in a cap, allowing for continuous, uninterrupted cooling throughout the treatment session (Rugo and Voigt, 2018). These have purported advantages of greater ease of use for clinical personnel, and greater comfort for patients (Shah et al., 2018). Automated scalp cooling systems include the DigniCap (Dignitana Inc., Dallas, TX) and Paxman Scalp Cooling System (Paxman Coolers Limited, Huddersfield, UK).

Although scalp cooling is the most widely used method for the prevention of CIA, its efficacy is variable and can be unpredictable (Komen et al., 2013; Shah et al., 2018). Furthermore, there is concern that scalp cooling may be associated with scalp metastasis due to lack of chemotherapy reaching tumor cells seeded in the scalp (Hayes, 2018).

U.S. Food and Drug Administration (FDA)
Many cooling devices are described by the U.S. Food and Drug Administration (FDA) as water circulating hot or cold pack. The FDA approves them through 510(k) and has listed them as Class II devices that are in the classification of Medical Devices/Physical Medicine Devices/Physical Medicine Therapeutic Devices. The FDA has determined that a water circulating hot or cold pack is a device intended for medical purposes that operates by pumping heated or chilled water through a plastic bag and that provides hot or cold therapy for body surfaces.

There are some cooling devices that have been classified by the FDA as compressible limb sleeve or intermittent, external pneumatic compression devices (e.g., NanoTherm and Vascutherm systems). The FDA 510(k) summary for these devices includes other intended uses in addition to cooling (e.g., reduction and control of edema including lymphedema and venous stasis ulcers) (FDA, 2006).

Passive cooling devices are described by the FDA as physical medicine devices, for use as daily assist devices. These are modified adaptors or utensils intended for medical purposes to assist a patient to perform a specific function. The FDA has classified these devices as Class I and has noted that they are exempt from the premarket approval notification procedures.

FDA—Scalp Cooling Systems
Two scalp cooling systems have been cleared through the FDA 510(k) process. The class II devices are regulated under 21 CFR 878.4360 and are assigned Product Code PMC (scalp cooling systems) and include:

Paxman Scalp Cooler: The Paxman Scalp Cooler (Paxman Coolers Limited, Huddersfield, UK) is indicated to reduce the likelihood of chemotherapy-induced alopecia (CIA) in cancer patients with solid tumors (FDA, 2018).

Contraindications listed in the FDA approval for Paxman scalp cooler include:

- Scalp cooling is contraindicated in pediatric patients.
- Scalp cooling is contraindicated in patients with:
  - An existing history of scalp metastases or the presence of scalp metastasis is suspected.
  - Cancers of the head and neck.
  - CNS malignancies (either primary or metastatic).
  - Cold sensitivity, cold agglutinin disease, cryoglobulinemia, cryofibrinogenemia, cold migraine, cold urticaria, and post-traumatic cold dystrophy.
  - Hematological malignancies (leukemia, non-Hodgkin and other generalized lymphomas) or hematological malignancies that are being treated for cure.
  - Imminent bone marrow ablation chemotherapy.
  - Imminent skull irradiation.
  - Previously received, or scheduled to undergo skull irradiation.
  - Scalp metastases have rarely been reported in the literature, but caution regarding their development has been a limitation for the broad-scale application of scalp cooling during chemotherapy. Theoretically, tumor cells that have seeded in the scalp might not receive adequate chemotherapy during hypothermia, thus allowing them to grow at a later date.
  - Severe liver or renal disease from any etiology who may not be able to metabolize or clear the metabolites of the chemotherapeutic agent.
  - Skin cancers including melanoma, squamous cell carcinoma, and Merkel cell carcinoma.
  - Small cell carcinoma of the lung.
  - Solid tumors that have a high likelihood for metastasis in transit.
  - Squamous cell carcinoma of the lung.

DigniCap Scalp Cooling System: The DigniCap® Scalp Cooling System (Dignitana Inc., Dallas, TX) is indicated to reduce the likelihood of chemotherapy-induced alopecia in cancer patients with solid tumors (FDA, 2017). The DigniCap Delta received FDA clearance in 2019 and is intended for use in the same population and with the same indications for use as its predicate device: DigniCap Scalp cooling system.

Contraindications of the DigniCap scalp cooling system include:

- The use of Dignicap is contraindicated in pediatric patients.
- The use of Dignicap is contraindicated in adult patients with:
  - cold sensitivity,
- cold agglutinin disease,
- cryoglobulinemia
- cryofibrinogenemia.
- Cold urticaria
- CNS malignancies (either primary or metastatic),
- squamous cell carcinoma of the lung,
- small cell carcinoma of the lung,
- cancers of the head and neck, skin cancers including melanoma, squamous cell carcinoma, and Merkel cell carcinoma
- hematological malignancies treated with curative intent by chemotherapy
- solid tumor malignancies with a high likelihood of metastases in transit
- patients who are scheduled for bone marrow ablation chemotherapy
- patients who are scheduled to undergo skull irradiation
- patients who have previously received skull irradiation

**Literature Review**

Although cold therapy has a long history as a therapeutic entity in the treatment of soft-tissue injury and in postoperative rehabilitation, the literature is conflicting on the efficacy of this treatment. In addition, there is insufficient evidence in the published, peer-reviewed scientific literature to demonstrate that the use of specialized devices that provide cooling and compression have a clinical benefit over the conventional, intermittent application of ice packs and wraps. Cooling devices, both passive or active pump-controlled devices, that provide cooling and compression have no additional clinical utility or impact on health outcomes than the use of ice or compression wraps. It does appear that such devices may offer ease of application and be more convenient.

Adie et al (2012) conducted a Cochrane review to evaluate the acute application of cryotherapy following total knee replacement (TKR) on pain, blood loss and function. The review included 11 randomized trials and one controlled clinical trial with 809 participants. The included studies had clinical heterogeneity in interventions and controls—utilizing cold with compression and no compression and cold therapy applied with devices and with application of ice. The inclusion criteria was randomized controlled trials or controlled clinical trials in which the experimental group received any form of cryotherapy, and was compared to any control group following TKR indicated for osteoarthritis. The authors found very low quality evidence from 10 trials (666 participants) that cryotherapy has a small benefit on blood loss, however, it was noted that this benefit may not be clinically significant. There was very low quality evidence from four trials (322 participants) that cryotherapy improved visual analogue score pain at 48 hours which was considered that this benefit may not be clinically significant. There was no difference between groups in adverse events (RR = 0.98, 95% CI, 0.28 to 3.47). There is low quality evidence from two trials (107 participants) for improved range of motion at discharge, but this benefit may not be clinically significant. There was no difference between groups in transfusion rate and knee function was not measured in any trial. No significant benefits were found for analgesia use, swelling or length of stay. Outcomes measuring quality of life or activity level were not reported. The authors concluded that the potential benefits of cryotherapy on blood loss, postoperative pain, and range of motion may be too small to justify its use, and the quality of the evidence was very low or low for all main outcomes. They noted that these findings need to be balanced against potential inconveniences and expenses of using cryotherapy. Well-designed randomized trials are required to improve the quality of the evidence.

Published randomized trials have not demonstrated the efficacy of a cryotherapy devices compared to the use of ice packs for knee surgery including for total knee arthroplasty (Su, et al., 2012), anterior cruciate ligament (ACL) reconstruction (Waterman, et al., 2012; Dervin, et al., 1998; Konrath, et al., 1996), and knee arthroscopy (Woolf, et al., 2008). A randomized study of 40 patients undergoing total shoulder arthroplasty (TSA) found no differences in pain control, quality of sleep, patient satisfaction, or narcotic usage were detected between cryotherapy and plain ice following TSA (Noyes, et al., 2018).

Bleakly et al. (2004) performed a systematic review of randomized, controlled trials to assess the evidence base for cryotherapy in the treatment of acute soft-tissue injury. Twenty-two studies of randomized, controlled trials were included in the review. Five different methods of cryotherapy were used in the studies: crushed or chipped ice, Cryo/Cuff or cold compressive devices, commercial ice machines, commercial/gel ice packs and ice
submersion. Five of the studies simply stated that an ice bag or pack was applied and eight studies used more than mode of cooling. It was noted that the duration and frequency of the treatments were not consistent across studies and had a wide range. Four studies compared two different methods of applying simultaneous compression and cryotherapy. The authors stated that due to the poor reporting of data, it was difficult to draw conclusions. Two studies did not provide adequate information on mode of cryotherapy, and all studies failed to specify the duration and frequency of ice application. The review concluded that many more high-quality studies are needed on this topic. Studies should focus on developing modes, durations and frequencies of ice application in order to optimize cryotherapy treatment during postoperative and rehabilitative care.

A systematic review of the literature (MacAuley, 2001) examined use of cryotherapy in acute soft tissue injury and attempted to produce evidence-based guidance on treatment. The review examined the effectiveness of ice in reducing tissue temperature, different methods of ice application, differing temperature, and duration to and the depth of the cooling effect. The study’s conclusion noted that the optimal method of ice application is wet ice applied directly to the skin through a wet towel and that the target temperature reduction is to 10–15 °C. While there is no evidence from the literature suggesting an optimal frequency or duration of treatment, it appears that repeated ice applications of 10 minutes each are effective. Most studies are not controlled for area of ice application, mode of application, depth of subcutaneous fat, method of calculating depth, or method of measuring temperature.

Literature Review—Cooling Devices for Multiple Sclerosis
The NASA/MS Cooling Study Group (Schwid, et al., 2003) conducted a multicenter, controlled double-blinded study to determine the effects of a single acute dose of cooling therapy and to determine whether effects are sustained during long-term use of a daily cooling garment. The study involved 84 patients with definite MS, mild to moderate deformity, and self-reported heat sensitivity, and used active cooling garments. The active cooling device from Lifetime Enhancement Technologies Inc. was used in this study. It was noted that body temperature declined with both the high dose and the sham, or low dose, cooling. It was also noted that the high dose cooling produced a small improvement, and the low-dose showed a trend toward improvement. The authors concluded that cooling therapy was associated with objectively measurable but modest improvements in motor and visual function, as well as persistent subjective benefits. Limitations of the studies include the small patient populations and lack of a comparator.

Several small cross-over studies evaluated effectiveness of cooling devices on the symptoms of MS (Reynolds, et al., 2011; Myer-Heim, et al., 2007; Beenakker, et al., 2001). These trials were preliminary, included small number or subjects, and noted that further studies were needed to assess the efficacy of cooling of symptoms of multiple sclerosis.

Literature Review—Scalp cooling for Scalp Cooling Devices for the Prevention of Chemotherapy-Induced Alopecia
Hayes published a medical technology directory report for scalp cooling devices for the prevention of chemotherapy-induced alopecia (CIA). Due to the large amount of recent published literature, a review of reviews methodology was adopted for this report. The evidence included in the report was based on one recent systematic review (SR) that included eight randomized controlled trials (RCTs) and ten nonrandomized controlled trials (CCTs) that evaluated scalp cooling relative to no scalp cooling for the prevention of CIA in cancer patients undergoing chemotherapy. Three subsequently published non-comparative prospective cohort studies were reviewed for safety data. Efficacy outcome measures included CIA and hair preservation. In the SR, a total of 52% (113/217) of patients in the RCTs and 72% (507/702) of patients in the CCTs had successful hair preservation with scalp cooling. A random-effects meta-analysis of all 18 studies with 1518 patients found a risk ratio for hair loss of 0.478 (95% CI, 0.373-0.613) with scalp cooling, a significant reduction. No subsequently published studies evaluating efficacy outcomes met inclusion criteria. The SR noted no systemic reactions to scalp cooling. The most common adverse events included cold intolerance, heavy cap weight, and mild and transient headache. Anxiety, nausea, dizziness, and chest pain were also reported. Cold caps, but not liquid thermal caps, were associated with cold thermal injuries. The number of thermal injuries was not reported. No scalp metastases were identified in reviewed patients in the SR, but studies were not designed to assess this outcome and may have been underpowered in terms of sample size and duration of follow-up. The single non-comparative study that evaluated scalp metastasis found no scalp metastases in patients who received scalp cooling over a median follow-up period of eight years. The overall quality of the evidence regarding the efficacy
and safety of scalp cooling for prevention of CIA was rated as low, due to individual study limitations. The report concluded that there was a high level of qualitative consistency among studies in the SR, which found that scalp cooling is more effective than no cooling for hair preservation, even though no quantitative conclusion about the size of that benefit is currently possible due to unexplained heterogeneity. The overall evidence suggests that there are no major complications related to scalp cooling and that most side effects are tolerable. No cases of scalp metastases were observed in the SR or in one non-comparative study in breast cancer patients. There is a need for additional research into the incidence of scalp metastases among patients who use scalp cooling.

Gianotti et al. (2019) conducted a prospective, observational study to assess the effectiveness of scalp cooling (SC) in daily clinical practice in three Italian oncology units. The study included 220 female early-stage breast cancer patients undergoing curative chemotherapy in combination with SC using the Paxman device. Effectiveness was defined as the severity of hair loss according to the Common Terminology Criteria for Adverse Events Version 4.0: Grade 0, no hair loss; Grade 1, <50% hair loss not requiring a wig; and Grade 2, ≥50% hair loss at each cycle and at completion of chemotherapy. The tolerability and safety were also evaluated. Two hundred women were evaluated and the overall success rate of SC (hair loss Grade 0-1) was 68%. Severe hair loss was avoided in 89% of women receiving taxane-based chemotherapy and in 78% of women receiving both anthracyclines and taxanes. Among women undergoing anthracycline-based chemotherapy, 47% experienced hair preservation. SC was well tolerated, as only 20 patients discontinued SC for reasons other than hair loss.

Kinoshita et al. (2019) conducted a non-randomized control trial to assess the efficacy of scalp-cooling devices in preventing chemotherapy-induced alopecia in Japanese breast cancer patients and investigated whether a scalp-cooling device improves hair volume recovery over a 12 weeks period after completing chemotherapy. The study included 48 patients and of them, 34 and 14 were sequentially allocated to the scalp-cooling group using the Paxman Hair Loss Prevention System and the control group, respectively. Scalp cooling was compared to no treatment. Scalp cooling was initiated 30 minutes prior to each chemotherapy infusion, and continued until at least 90 minutes following completion. More than 50% of patients in each group had stage II breast cancer (scalp-cooling group: 53.1%; control group: 64.3%), more than 90% received adjuvant chemotherapy (scalp-cooling group: 96.9%; control group: 92.9%), and more than 60% were treated with a docetaxel/cyclophosphamide regimen (scalp-cooling group: 75.0%; control group: 64.3%). There were more patients judged to have no alopecia at the end of chemotherapy in the scalp-cooling group than in the control group (26.7% [8/30] vs. 0% [0/13]; p=0.011). The proportion of patients with alopecia who experienced an increase in hair volume of ≥50% within 12 weeks duration after chemotherapy was 85.7% (24/28) in the scalp-cooling group and 50.0% (6/12) in the control group. No patient developed serious adverse events related to the scalp-cooling device.

Vasconcelos et al. (2018) conducted a prospective, observational study of women with breast cancer undergoing chemotherapy and scalp cooling using a Paxman device. The study included 131 participants with 74% (n=97) receiving anthracycline/taxane-based chemotherapy and 26% (n=34) receiving taxane-monotherapy based chemotherapy. The primary efficacy end points were: successful hair preservation (no hair loss; <30% hair loss not requiring a wig; or <50% hair loss not requiring a wig) at the completion of chemotherapy. Secondary end points included adverse effects such as headache, pain, nausea or dizziness. Hair preservation was successful in 102 women who underwent scalp cooling (71.0%; 95% CI = 63-79%); 93 participants experienced <50% hair loss and not requiring a wig. The success rate was significantly different among the different chemotherapy regimens, with the highest success rates among those receiving taxane-monotherapy-based therapy (88.0% success rate) followed by those receiving weekly anthracycline/taxane-based therapy (76.0% success rate) and three-weekly anthracycline/taxane-based therapy (59.0% success rate). The low number of patients receiving carboplatine/anthracycline combination (n=5) precluded analysis of individual success rates. Overall, 7.0% of participants withdrew from the intervention due to adverse effects (two due to headaches, one due to nausea and six due to discomfort during the intervention).

Shah et al. (2018) conducted a review and side-by-side comparisons of controlled and randomized clinical trials evaluating scalp hypothermia for the prevention of chemo induced alopecia (CIA). Sixteen original studies including ten controlled clinical trials (CCT) and eight randomized clinical trials (RCT) were included. The ten CCTs included 1,107 patients; 702 patients received scalp cooling, 195 of which (28%) experienced CIA as defined by individual study assessment criteria. Of patients that did not undergo scalp cooling, 297 of 392 patients (76%) experienced CIA. The review indicated that the results demonstrated that patients receiving scalp
cooling were 2.7 times less likely to experience CIA, and the differences between the two groups were statistically significant in all but two of the nine CCTs. The eight RCTs included a total of 375 patients: 217 patients received scalp cooling, 113 of which (52%) achieved hair preservation as defined by individual study assessment criteria. In contrast, only 15 of 158 patients (9.5%) who did not undergo scalp cooling achieved hair preservation. The review noted that these results showed that patients receiving scalp cooling were 5.5 times more likely to achieve hair preservation, and the difference in the incidence of hair preservation between intervention and control groups was statistically significant in seven of the eight RCTs. The authors concluded that as a whole, results from CCTs and RCTs to date suggest that scalp hypothermia represents an effective preventative measure for CIA, but the current application needs to be evaluated and optimized for better results. Furthermore, at a basic level, additional studies are needed to more clearly elucidate the fundamental pathophysiology of CIA. Current studies have almost all focused on effectiveness with arbitrary choices for cooling times and temperatures. Before guidelines can be written, proper additional research is needed including studies on time and temperature control would also increase the outcomes, as might addition of topicals during scalp cooling.

Rugo et al. (2018) conducted a systematic review and meta-analysis to examine the effects of scalp cooling on the end point of alopecia in randomized controlled trials. Any type of scalp cooling system was included in the analysis and each scalp cooling system was in place approximately 15 to 20 minutes before, during, and at 30 to 60 minutes after chemotherapy. All of these studies except for two used older scalp cooling technology (e.g., frozen caps) rather than the more recent technologies (e.g., DigniCap Scalp Cooling System or Paxman). Two studies used the Paxman system. Most patients in all of these studies were treated with anthracyclines (doxorubicin, epirubicin or taxanes) for several cycles. The primary outcome measure evaluated was the extent of alopecia during and after chemotherapy regimens for treating cancer with the more common means for evaluating alopecia being a grade scale from 0 to 3, with a grade of “0” being no alopecia (0% alopecia); a grade of 1 being > 0% to < 25% alopecia (minimal alopecia); grade of 2 being > 25% to < 50% alopecia (moderate alopecia) and; a grade of 3 being > 50% alopecia (severe alopecia requiring a wig). Secondary outcomes were noted such as adverse events, which included headache, cold sensation, and intolerability of cold cap (with requirement for removal), and quality of life (QoL) were evaluated. Ten studies were included in the analysis comprised of 654 patients. Most were patients with breast cancer including 432 patients [66%] who were mainly receiving anthracyclines. For the binary outcome of < 50% versus > 50% alopecia, the use of scalp cooling reduced relative risk (RR) of alopecia by 43% (RR, 0.57; 95% CI, 0.45-0.72; I2 = 11%; p<.00001). For ordinal outcomes (alopecia on a scale of 0-3), use of scalp cooling significantly reduced alopecia (MD, -0.80; 95% CI, -1.19 to -0.41; I2 = 0%; p<.0001). The quality of the evidence was graded as moderate. Only one study reported on QoL assessments using the European Organization for Research and Treatment for Cancer Quality of Life Questionnaire—Core 30, Hospital Anxiety and Depression Scale, and Body Image Scale.28 In examining between group differences using the Kruskal–Wallis test, there were no statistical differences on any of these instruments.

Nangia, et al. (2017) conducted a randomized multicenter trial to assess whether a scalp cooling device is effective at reducing chemotherapy-induced alopecia and to assess adverse treatment effects (Scalp Cooling Alopecia Prevention [SCALP] trial). The study included 182 women with breast cancers who were randomized to scalp cooling with scalp cooling device (Paxman) (n = 119) or control (n = 63) Scalp cooling was done using a scalp cooling device. The primary efficacy end points were successful hair preservation assessed using the Common Terminology Criteria for Adverse Events version 4.0 scale (grade 0 [no hair loss] or grade 1 [<50% hair loss not requiring a wig] were considered to have hair preservation) at the end of four cycles of chemotherapy by a clinician unaware of treatment assignment, and device safety. Secondary end points included wig use and scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire—Core 30, Hospital Anxiety and Depression Scale, and a summary scale of the Body Image Scale. At the time of the interim analysis, 142 participants were evaluated with 36% (n = 51) that had received anthracycline-based chemotherapy and 64% (n = 91) had received taxane-based chemotherapy. Successful hair preservation was found in 48 of 95 women with cooling (50.5%; 95% CI, 40.7%-60.4%) compared with 0 of 47 women in the control group (0%; 95% CI, 0%-7.6%) (success rate difference, 50.5%; 95% CI, 40.5%-60.6%). There were no statistically significant differences in changes in any of the scales of quality of life from baseline to chemotherapy cycle 4 among the scalp cooling and control groups. Only adverse events related to device use were collected; 54 adverse events were reported in the cooling group, all grades 1 and 2. There were no serious adverse device events. The authors concluded that among women with stage I to II breast cancer receiving chemotherapy with
taxane, anthracycline, or both, those who underwent scalp cooling were significantly more likely to have less than 50% hair loss after the fourth chemotherapy cycle compared with those who received no scalp cooling and that further research is needed to assess longer-term efficacy and adverse effects.

Rugo et al. (2017a) conducted a prospective cohort study to evaluate whether use of a scalp cooling system is associated with a lower amount of hair loss among women receiving specific chemotherapy regimens for early-stage breast cancer and to assess related changes in quality of life. The study included women with stage I or II breast cancer receiving adjuvant or neoadjuvant chemotherapy regimens excluding sequential or combination anthracycline and taxane (106 patients in the scalp cooling group and 16 in the control group; 14 matched by both age and chemotherapy regimen). The main outcome was self-estimated hair loss using the Dean scale and was assessed four weeks after the last dose of chemotherapy by unblinded patient review of five photographs. A Dean scale score of 0 to 2 (≤50% hair loss) was defined as treatment success. A positive association between scalp cooling and reduced risk of hair loss would be demonstrated if 50% or more of patients in the scalp cooling group achieved treatment success, with the lower bound of the 95% CI greater than 40% of the success proportion. Quality of life was assessed at baseline, at the start of the last chemotherapy cycle, and one month later. Median follow-up was 29.5 months. No participants in the scalp cooling group received anthracyclines. Hair loss of 50% or less (Dean score of 0-2) was seen in 67 of 101 patients (66.3%; 95% CI, 56.2%-75.4%) in the scalp cooling group vs 0 of 16 patients (0%) in the control group (p<.001). Three of five quality-of-life measures were significantly better one month after the end of chemotherapy in the scalp cooling group. Of patients who underwent scalp cooling, 27.3% (95% CI, 18.0%-36.6%) reported feeling less physically attractive compared with 56.3% (95% CI, 31.9%-80.6%) of patients in the control group (p=.02). Of the 106 patients in the scalp cooling group, four (3.8%) experienced the adverse event of mild headache and three (2.8%) discontinued scalp cooling due to feeling cold. The authors concluded that among women undergoing non-anthracycline-based adjuvant chemotherapy for early-stage breast cancer, the use of scalp cooling vs no scalp cooling was associated with less hair loss at four weeks after the last dose of chemotherapy and that further research is needed to assess outcomes after patients receive anthracycline regimens, longer-term measures of alopecia, and adverse effects.

Rujo et al. (2017b) conducted a systematic review and meta-analysis of longitudinal studies to retrospectively evaluate the effect of scalp cooling versus no scalp cooling on the risk of scalp metastasis in patients treated for breast cancer with chemotherapy. The review included articles which evaluated patients treated for breast cancer with chemotherapy and, with and without the use of scalp cooling technology and, examined the longer-term sequelae of this therapy (with identified follow-up timeframes) including scalp metastasis. Ten studies quantified the incidence of scalp metastasis with scalp cooling over time. For scalp cooling, 1959 patients were evaluated over an estimated mean time frame of 43.1 months. For no scalp cooling, 1238 patients were evaluated over an estimated mean time frame of 87.4 months. The incidence rate of scalp metastasis in the scalp cooling group versus the no scalp cooling group was 0.61% (95% CI 0.32–1.1%) versus 0.41% (95% CI 0.13–0.94%); p=0.43. The authors concluded that the incidence of scalp metastases was low regardless of scalp cooling and that this suggests that scalp cooling does not increase the incidence of scalp metastases.

Professional Societies/Organizations:

**National Comprehensive Cancer Network™ (NCCN™):** The NCCN (2019) guidelines for Breast Cancer include the following recommendation:

Consider scalp cooling to reduce incidence of chemotherapy-induced alopecia for patients receiving neoadjuvant/adjuvant chemotherapy. Results may be less effective with anthracycline regimens.

Level 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**National Multiple Sclerosis Society (NMSS):** NMSS, in a clinical bulletin regarding complementary and alternative medicine in MS, notes that, “Limited studies indicate that several CAM therapies may be beneficial for people with MS. Cooling therapy, which involves the use of cooling suits, may improve some MS symptoms.” (NMSS, 2010)

**Centers for Medicare & Medicaid Services (CMS)**

- National Coverage Determinations (NCDs): Scalp Hypothermia During Chemotherapy to Prevent Hair Loss (110.6). This is a longstanding NCD; the effective date is not posted. The Coverage Policy is broader in scope than the NCD. Refer to the CMS NCD table of contents link in the reference section.
• Local Coverage Determinations (LCDs): Cold Therapy (L33735) (2017). Refer to the CMS LCD table of contents link in the reference section.

Use Outside of the US
National Collaborating Centre for Chronic Conditions (NCC-CC) (United Kingdom): NCC-CC published guidelines for diagnosis and management of MS (2014). Treatment with body cooling is not included in the recommendations.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Not Medically Necessary/Convenience Item when used to report cold therapy units or cooling devices, including both passive and active pump-controlled cooling and compression devices:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E0218</td>
<td>Fluid circulating cold pad with pump, any type</td>
</tr>
<tr>
<td>E0236</td>
<td>Pump for water circulating pad</td>
</tr>
<tr>
<td>E1399</td>
<td>Durable medical equipment, miscellaneous</td>
</tr>
</tbody>
</table>

Considered Experimental/Investigational/Unproven when used to report a cooling device/cooling garment for the treatment of multiple sclerosis:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>E1399</td>
<td>Durable medical equipment, miscellaneous</td>
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</tbody>
</table>

Considered Not Medically Necessary when used to report scalp cooling device for prevention of chemotherapy-induced alopecia:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
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References


