BlueCross BlueShield of Alabama

Name of Policy:

Low-Level Laser and High-Power Laser Therapies

Policy #: 270 Latest Review Date: July 2018

Category: Therapy Policy Grade: B

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Low-level laser therapy (LLLT), also called photobiomodulation, is being evaluated to treat various conditions, including, among others, oral mucositis, myofascial pain, joint pain, lymphedema, and chronic wounds.

Oral Mucositis

Oral mucositis describes inflammation of the oral mucosa and typically manifests as erythema or ulcerations that appear 7 to 10 days after initiation of high-dose cancer therapy. Oral mucositis can cause significant pain and increased risk of systemic infection, dependency on total parenteral nutrition, and use of narcotic analgesics.

Treatment

Treatment planning may also need to be modified due to dose-limiting toxicity. There are a number of interventions for oral mucositis that may partially control symptoms, but none is considered a criterion standard treatment. When uncomplicated by infection, oral mucositis is self-limited and usually heals within 2 to 4 weeks after cessation of cytotoxic chemotherapy. Low-level laser therapy (LLLT) has been used in cancer therapy–induced oral mucositis in patients treated with radiotherapy and/or chemotherapy and hematopoietic cell transplantation.

Musculoskeletal and Neurologic Disorders

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy and the most commonly performed surgery of the hand. The syndrome is related to the bony anatomy of the wrist. The carpal tunnel is bound dorsally and laterally by the carpal bones and ventrally by the transverse carpal ligament. Through this contained space run the 9 flexor tendons and the median nerve. Therefore, any space-occupying lesion can compress the median nerve and produce the typical symptoms of CTS-pain, numbness, and tingling in the distribution of the median nerve. Symptoms of more severe cases include hypesthesia, clumsiness, loss of dexterity, and weakness of pinch. In the most severe cases, patients experience marked sensory loss and significant functional impairment with thenar atrophy.

Treatment

Mild-to-moderate cases of CTS are usually first treated conservatively with splinting and cessation of aggravating activities. Other conservative therapies include oral steroids, diuretics, nonsteroidal anti-inflammatory drugs, and steroid injections into the carpal tunnel itself. Patients who do not respond to conservative therapy or who present with severe CTS with thenar atrophy may be considered candidates for surgical release of the carpal ligament, using either an open or endoscopic approach. LLLT is also used to treat CTS.

Low-Level Laser Therapy

LLLT is the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and power between 5 and 500 MW. (By comparison, lasers used in surgery typically use 300 W.) When applied to the skin, LLLT produces no sensation and does not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect on tissue healing is unknown; hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

LLLT is being evaluated to treat a wide variety of conditions, including soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, joint pain, and lymphedema.

Policy:

Low level laser therapy (LLLT), also known as cold laser therapy or class III laser; high-power laser therapy (HPLT), also known as class IV therapeutic laser; and laser acupuncture do not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational** for **ALL** indications, including, but not limited to:

- Carpal tunnel syndrome
- Chronic headache
- Temporomandibular joint dysfunction
- Low back pain
- Fibromyalgia
- Other painful musculoskeletal disorders
- Chronic non-healing wounds
- Neurological dysfunctions
- Smoking cessation
- Weight loss/Appetite suppression
- Trismus
- Raynaud's phenomenon
- Chronic neck pain
- Lateral epicondylitis (tennis elbow)
- Arthritis conditions
- Plantar fasciitis
- Shoulder pain
- Knee pain
- Rheumatoid arthritis
- Lymphedema
- Myofascial Pain
- Oral Mucositis

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature search was performed through April 26, 2018. The following is a summary of the key findings to date.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Prevention of Oral Mucositis

Clinical Context and Therapy Purpose

The purpose of low-level laser therapy (LLLT) in patients who have oral mucositis due to some cancer treatments and/or hematopoietic cell transplantation (HCT) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of LLLT improve the health outcomes in those who have oral mucositis due to some cancer treatments and/or HCT?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is those who have oral mucositis due to some cancer treatments and/or HCT.

Interventions

The therapy being considered is LLLT.

Comparators

The following therapies are currently being used: conservative therapy (e.g., oral hygiene, hydration) and pharmacologic agents.

Outcomes
The general outcomes of interest are reductions in symptoms and morbidity.

Timing
The effects of LLLT to promote healing are expected to occur from weeks to months.

Setting
LLLT is provided in an outpatient setting and may be administered by physical therapists and other practicing alternative medicine.

Systematic Reviews
In 2014, the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) issued guidelines that reiterated findings from their 2012 systematic review recommending LLLT for the prevention of oral mucositis in patients receiving HCT conditioned with high-dose chemotherapy and for patients undergoing head and neck radiotherapy, without concomitant chemotherapy. The 2014 systematic review included 24 trials on a variety of prophylactic treatments. Recommendations for the use of LLLT for prevention of oral mucositis in patients receiving HCT were based on what reviewers considered to be the well-designed, placebo-controlled, randomized trial by Schubert et al (2007), together with "weaker evidence" from 3 observational studies that showed positive results. This phase 3 trial was double-blind and sham-controlled evaluating 70 patients.2 Patients were randomized to 650 nm laser, 780 nm laser, or placebo. Patients in the 650-nm laser group were more likely to have received a total body irradiation-containing regimen than the other 2 groups; otherwise, the groups were comparable. LLLT began on the first day of conditioning and continued for 3 days posttransplant. Of the 70 patients, 47 (67%) had complete or nearly complete mucositis measurements over time; the average number of visits per patient was similar among the 3 groups. The difference between groups in mean oral mucositis scores was greatest at day 11 (650 nm, 16.7; 780 nm, 20.6; placebo, 24.3), but this difference between the 650-nm group and placebo group was not statistically significant (p=0.06). Patient-specific oral mucositis scores differed significantly between the 2 groups only when adjusted for total body irradiation exposure. Of the 70 patients in the trial, 17 (24%) were assessed for oral pain. With group sizes of 5 and 6, the 650-nm group had significantly lower patient-specific average pain scores (15.6) than the placebo group (47.2). No adverse events from LLLT were noted. Trial limitations included lack of statistically significant findings for the primary outcome measure and a very small percentage of patients with pain assessments. Overall, as relates to the 3 observational studies, reviewers noted that, due to the range of laser devices and variations in individual protocols, results of each study applied exclusively to the cancer population studied and the specific wavelength and settings used.

Additional systematic reviews have been published since the 2012 MASCC/ISOO systematic review. Oberoi et al (2014) reported on a systematic review and meta-analysis of 18 RCTs comparing LLLT with no treatment or placebo for oral mucositis. Eight RCTs assessed patients undergoing HCT, 8 evaluated head and neck cancer patients receiving radiotherapy or chemoradiation, and the rest studied patients with other conditions receiving chemotherapy. Reviewers used the Cochrane risk of bias tool to evaluate the RCTs. Most were considered at low risk of bias on most domains. For example, 68% were at low risk of bias for blinding of

patients and personnel, and 89% were at low risk of bias on incomplete outcome data. The primary outcome measure for the review was the incidence of severe mucositis. Ten studies (n=689 patients) were included in a pooled analysis for this outcome. The overall incidence of severe mucositis (grades 3-4) decreased with prophylactic LLLT, with a relative risk of 0.37 (95% confidence interval [CI], 0.20 to 0.67; p=0.001). Moreover, the absolute risk reduction in the incidence of severe mucositis (-0.35) significantly favored LLLT (95% CI, -0.48 to -0.21; p<0.001). Among secondary outcomes, LLLT also significantly reduced the overall mean grade of mucositis (standardized mean difference, -1.49; 95% CI, -2.02 to -0.95), duration of severe mucositis (weighted mean difference [WMD], -5.32; 95% CI, -9.45 to -1.19), and incidence of severe pain as measured on a visual analog scale (VAS; relative risk, 0.26; 95% CI, 0.18 to 0.37). In a subgroup analysis of the primary outcome (incidence of severe mucositis), the investigators did not find a statistically significant interaction between the type of condition treated and the efficacy of LLLT.

Randomized Controlled Trials

Two of the larger RCTs evaluating LLLT for prevention of oral mucositis were published by Gautam et al (2012). One reported on LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.7 The other reported on LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients. There is an apparent overlap in patients in these 2 reports, with the head and neck cancer study including the 121 patients with a primary tumor site in the oral cavity. Patients in these studies received LLLT before radiotherapy at 66 gray delivered daily in 33 fractions, 5 days per week, and concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm2, and a dosage of 3 to 3.5 J. In the report on oral cancer, LLLT before radiotherapy led to significant reductions in the incidence of severe oral mucositis (29% vs 89%) and its associated pain (18% vs 71%, with a VAS score >7), opioid analgesic use (7% vs 21%), and total parenteral nutrition (30% vs 39%), all respectively, during the last weeks of chemoradiotherapy. LLLT also reduced the duration of severe oral mucositis (4.07 days vs 13.96 days), severe pain (5.31 days vs 9.89 days), and total parenteral nutrition (14.05 days vs 17.93 days), all respectively. In the 221 patients treated for head and neck cancer, LLLT led to significant reductions in the incidence and duration of severe oral mucositis (8.19 days vs 12.86 days) and its associated pain (VAS score, 4 vs 7), total parenteral nutrition (45.0% vs 65.5%), and opioid analgesic use (9% vs 26% for step III), all respectively. Gautam et al (2013) assessed patient-reported on outcomes from the same study of 221 head and neck cancer patients using the Oral Mucositis Weekly Questionnaire-Head and Neck and the Functional Assessment of Cancer Treatment-Head and Neck questionnaire. Patients received LLLT as described above. Patients in the LLLT group reported significantly better outcomes than the placebo group, with lower scores on both the Oral Mucositis Weekly Questionnaire-Head and Neck (p<0.001) and Functional Assessment of Cancer Treatment-Head and Neck questionnaire (p<0.05).

In 2015 and 2016, 3 relatively small (i.e., each <50 patients), double-blind, sham-controlled, randomized trials on prevention of oral mucositis in patients undergoing cancer treatment were published. Gautam et al (2015) reported on 46 patients with head and neck cancer scheduled for radiotherapy and found significant reductions in the incidence and duration of severe oral mucositis (p=0.002) and severe pain (p=0.023) after LLLT vs sham. Oton-Leite (2015) reported on 30 head and neck cancer patients undergoing chemoradiation and found that oral mucositis

grades were significantly lower in the LLLT group than in the control group at the week 1, 3, and 5 evaluations. For example, at the last clinical evaluation (week 5), the rates of grade 3 oral mucositis were 25% in the LLLT group and 54% in the control group. Ferreira et al (2016) evaluated 36 patients with hematologic cancer undergoing HCT. The overall incidence of oral mucositis did not differ significantly between groups (p=0.146). However, the rate of severe oral mucositis (grade 3 or 4) was significantly lower in the laser group (18%) than in the control group (61%; p=0.015).

Section Summary: Prevention of Oral Mucositis

The literature on LLLT for the prevention of oral mucositis includes several systematic reviews, including a 2012 review by MASCC/ISOO, with a resulting recommendation for LLLT for adults receiving HCT conditioned with high-dose chemotherapy. Review of the key study evaluated by the MASCC/ISOO investigators for this recommendation revealed limitations that included statistically nonsignificant findings for the primary outcome measure. The MASCC/ISOO recommendation for LLLT for preventing oral mucositis in patients undergoing radiotherapy for head and neck cancer was based on lower level evidence. A 2014 systematic review of LLLT for prevention of oral mucositis included 18 RCTs, generally considered at low risk of bias, and found statistically significantly better outcomes with LLLT than with control conditions on primary and secondary outcomes. Also, 3 double-blind RCTs published in 2015 and 2016 found significantly better outcomes in patients undergoing LLLT compared with sham treatment before or during cancer treatment.

Musculoskeletal and Neurologic Disorders

Clinical Context and Therapy Purpose

The purpose of LLLT in patients who have various musculoskeletal and neurologic disorders is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of LLLT improve the health outcomes in those who have various musculoskeletal and neurologic disorders?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is those who have various musculoskeletal and neurologic disorders.

Interventions

The therapy being considered is LLLT.

Comparators

The following therapies are currently being used: conservative therapy (e.g., physical therapy, exercise), pharmacologic agents, and surgery.

Outcomes

The general outcomes of interest are pain relief and functional improvements.

Timing
The effects of LLLT to promote healing or pain relief are expected to occur from weeks to months.

Setting
LLLT is provided in an outpatient setting and may be administered by physical therapists and other practicing alternative medicine.

Carpal Tunnel Syndrome
A TEC Assessment (2010) evaluated LLLT for carpal tunnel syndrome and chronic neck pain. For inclusion in the assessment, studies had to: be published in a peer-reviewed journal; be randomized, sham-controlled trials, and, if adjunctive therapies were used, they were applied to both groups; measure outcomes at least two weeks beyond the end of the treatment period; and, for neck pain studies, be studies of patients with chronic pain. Four of the studies of carpal tunnel syndrome discussed below met the inclusion criteria for the TEC Assessment. TEC concluded that the studies have serious limitations including small sample size and limited follow-up, and no one study is so methodologically sound as to provide definitive results.

In 2016, Li et al published a meta-analysis of RCTs on LLLT for CTS. Reviewers identified 7 RCTs. Meta-analyses evaluated outcomes for hand grip strength; pain measured by a VAS, symptom severity scores, and functional status scores. Short-term follow-up was defined as less than 6 weeks after treatment and long-term follow-up as at least 12 weeks after treatment. For 6 of the 8 meta-analyses, there were not statistically significant between-group differences in outcomes. They included short-term assessment of hand grip, short-term assessment of pain (VAS), and short- and long-term assessment of symptom severity and functional status scores. Meta-analyses found stronger hand grip (3 studies) and greater improvement in VAS scores (2 studies) at the long-term follow-up in the LLLT group than in the control. Most data for these 2 positive analyses were provided by a single RCT (Fusakul et al [2014]). Reviewers concluded that additional high-quality trials with similar LLLT protocols would be needed to confirm that the intervention significantly improves health outcomes.

Section Summary: Carpal Tunnel Syndrome
A number of RCTs and several systematic reviews have been published. The most recent systematic review (2016) identified 7 RCTs. Meta-analyses did not find a significant benefit of LLLT compared with a control condition for most of the outcome measures (6 of 8). Previously in 2010, a TEC Assessment concluded that the evidence from sham-controlled RCTs was insufficient. More recent RCTs have not found that LLLT significantly improves outcomes.

Neck Pain
The 2010 TEC Assessment included 6 trials of LLLT for chronic neck pain and found inconsistent results. In the largest study by Chow et al, 90 patients were randomized to active LLLT or sham treatment. At 5 weeks after the 7-week treatment period, patients in the active treatment group reported a 2.7 point improvement in VAS pain versus a 0.3 point worsening for the sham group. A calculated mean improvement of 43.8% was reported by the active LLLT group while the sham-treated group improved by 2.1%. TEC noted that baseline VAS pain scores were significantly higher in the active treatment group possibly biasing results in favor of

LLLT. Overall, the authors concluded that the trials were characterized by small sample sizes, limited statistical power and limited long-term follow-up and thus the evidence was insufficient.

In a 2013 systematic review and meta-regression, Gross et al evaluated 17 trials on LLLT for neck pain. Ten of these trials were found to demonstrate high risk of bias. Two trials consisting of 109 subjects were considered to be of moderate quality and found LLLT produced better outcomes than placebo for chronic neck pain treatment. Other evidence showed improved outcomes with LLLT compared to placebo for acute neck pain, acute radiculopathy and cervical osteoarthritis but was considered to be low quality. There was conflicting evidence on chronic myofascial neck pain.

Section Summary: Neck Pain
A number of RCTs and several systematic reviews have been published. A 2013 systematic review identified 17 trials. Only 2 trials considered moderate quality found that LLLT led to better outcomes than placebo for chronic neck pain. Other trials were considered low quality. A 2010 TEC Assessment found conflicting evidence. While some studies showed positive benefits with LLLT over placebo, others did not. Additionally, laser types, dosages, and treatment schedules varied in the available evidence.

Subacromial Impingement Syndrome
Several RCTs evaluating LLLT for treatment of subacromial impingement have been published. Two sham-controlled studies, by Yeldan et al (2009) and by Dogan et al (2010) did not find statistically significantly better pain or function outcomes with active treatment vs sham. A third RCT, published by Abrisham et al in 2011, compared exercise plus pulsed LLLT or sham laser 5 times per week for 2 weeks in 80 patients with subacromial syndrome (rotator cuff and biceps tendinitis). At the conclusion of the treatment period, both groups showed improvement in VAS for pain and shoulder ROM. The improvement was significantly better for the active LLLT group than the sham laser group for VAS (4.4 vs 2.9), and all measures of ROM (active and passive flexion, abduction, external rotation). The durability of this effect was not assessed.

Other RCTs did not show statistically significant benefit of LLLT versus conservative treatment. In a 2009 study designed to assess the effectiveness of LLLT in patients with subacromial impingement syndrome, 44 patients were randomized in equal numbers to receive a 12-week home exercise program with or without LLLT. Outcome measures of night pain, shoulder pain, and disability index (SPADI), and University of California-Los Angeles (UCLA) end-result scores were assessed at the second and twelfth week of intervention. Both groups showed significant reductions in night pain and SPADI at 2 and 12-week assessments, but the differences between groups were not statistically significant.

In 2011, Calis et al randomized 52 patients with subacromial impingement syndrome to LLLT, US, or exercise. Patients were treated five days a week for three weeks with hotpack+ultrasound+exercise, hotpack+laser+exercise, or hotpack+exercise. All three groups showed improvement from baseline to posttreatment in pain at rest, ROM, and function. There were no significant differences between the groups.

Section Summary: Subacromial Impingement
The literature on LLLT for subacromial syndrome consists of several RCTs. Most trials did not show a significant benefit of LLLT compared with sham treatment or with an alternative intervention (e.g. exercise).

Adhesive Capsulitis (Frozen Shoulder)
A 2014 Cochrane review evaluated LLLT and other electrotherapy modalities for frozen shoulder. The review found limited evidence to draw conclusions on the effectiveness of electrotherapy modalities for frozen shoulder. Only 1 RCT of 40 patients compared LLLT with placebo. This trial administered LLLT for 6 days. On the sixth day, LLLT was considered to have some improvement in a global assessment of treatment success when compared with placebo. However, this study was considered to be of low quality and the small size and short follow-up limited interpretation of results. Another RCT on LLLT discussed in the Cochrane review by Stergioulas (2008) was considered to be of moderate quality. In this study**,** 63 patients with frozen shoulder were included in an RCT comparing an eight-week program of LLLT (n=31) or placebo (n=32). Both groups also participated in exercise therapy. Compared to the sham group, the active laser group had a significant decrease in overall, night, and activity pain scores after 4 weeks and 8 weeks of treatment, and at the end of 8 more weeks of follow-up. At the same time intervals, a significant decrease in shoulder pain, disability index (SPADI) scores, and Croft shoulder disability questionnaire scores was observed, while a significant decrease in disability of arm, shoulder, and hand questionnaire (DASH) scores was observed at eight weeks of treatment and at 16 weeks' post-randomization; and a significant decrease in health assessment questionnaire scores was observed at 4 weeks and 8 weeks of treatment.

Section Summary: Adhesive Capsulitis
A Cochrane review on treatments for adhesive capsulitis identified 2 RCTs on LLLT for adhesive capsulitis and, due to the small number of trials and study limitations, concluded that the evidence was insufficient to draw conclusions on the effectiveness of LLLT for adhesive capsulitis.

Temporomandibular Joint Pain
Several systematic reviews and meta-analyses of RCTs on LLLT for temporomandibular joint (TMJ) pain have been published. A 2015 systematic review by Chen et al published a meta-analysis of pain and functional outcomes after LLLT for TMJ pain. Fourteen placebo-controlled RCTs were identified. Ten trials provided data on pain, measured by a visual analog scale (VAS). A pooled analysis of these studies found no significant difference between active treatment and placebo on the VAS at final follow-up (weighted mean difference [WMD], -19.39; 95% CI, -40.80 to 2.03; p=0.08). However, meta-analyses did find significantly better functional outcomes (i.e., maximum active mouth opening, maximum passive mouth opening). For example, the mean difference in maximum active mouth opening, active treatment versus placebo, at final follow-up was a mean difference (MD) of 4.18 (95% CI, 0.73 to 7.63).

In 2014, Chang et al published a meta-analysis of seven RCTs on LLLT for TMJ pain. RCTs included in the review compared LLLT with no treatment or placebo. Six studies with a total of 223 patients were eligible inclusion in the meta-analysis. The number of treatment sessions

ranged from four to 20. The pooled effect size of pain relief using the VAS was a mean decrease of 0.6 (95% CI, -0.47 to -0.73).

In a double-blind, placebo-controlled randomized trial, Shobha et al (2017) investigated the effectiveness of LLLT in patients with TMJ pain. Forty TMJ patients were evenly randomized to an active or a placebo group. Treatment included 2 to 3 weekly sessions of LLLT for a total of 8 sessions. Patients were evaluated at baseline, after treatment, and at a 30-day follow-up. Both groups experienced pain reduction at all evaluation points. The most significant pain reduction was reported at the 30-day follow-up (p=0.001). There were no significant differences between groups at baseline (p=0.214), final session (p=0.000), or the 30-day follow-up (p=0.230). For a secondary outcome (the ability to open one's mouth), while both groups showed improvement, the difference between groups was not significant (p=0.330). Therefore, LLLT was determined to have no greater impact on healing or pain reduction over placebo. A study limitation is that MRI was not used, which is the traditional method for diagnosing TMJs.

Section Summary: Temporomandibular Joint Pain
There are a number of RCTs on LLLT for TMJ pain and several systematic reviews. Meta-analyses of these trials had mixed findings. The most recent meta-analysis, which included 14 placebo-controlled randomized trials, did not find a statistically significant impact of LLLT on pain, but did find that LLLT significantly improved function outcomes (e.g., mouth opening). RCTs have not compared the impact of LLLT with physical therapy on health outcomes.

Low Back Pain
In 2015, Huang et al published a systematic review of RCTs on LLLT for treatment of nonspecific chronic low back pain. The review included trials comparing LLLT and placebo that reported pain and/or functional outcomes and reported a PEDro quality score. Seven trials with a total of 394 patients were included (202 assigned to LLLT and 192 assigned to placebo). Six of the seven trials were considered high quality (i.e., a PEDro score of at least seven out of 11 possible points). Primary outcomes of interest were post-treatment pain measured by VAS and disability measured by the Oswestry Disability Index (ODI). Range of motion and change in pain scores were secondary outcomes. In pooled analyses of study data, the authors found a statistically significant benefit of LLLT on pain outcomes, but not disability or range of motion. For the primary outcome post-treatment pain scores, in a meta-analysis of all seven trials, mean VAS was significantly lower in the LLLT compared with the placebo group (WMD = -13.57; 95% CI, -17.42 to -9.72). In a meta-analysis of four studies reporting the other primary outcome, ODI, there was not a statistically significant difference between LLLT and placebo groups (WMD = -2.89; 95% CI, -7.88 to 2.29). Outcomes were only reported immediately after treatment.

A number of RCTs and several systematic reviews of RCTs have been published. Most recently, Glazov et al (2016) published a meta-analysis of blinded sham-controlled trials evaluating LLLT for treatment of chronic low back pain. Fifteen RCTs (total n=1039 patients) met reviewers' eligibility criteria. Reviewers found that 3 of the 15 trials were at higher risk of bias (using a modified Cochrane risk of bias tool), mainly due to lack of blinding. The primary outcomes of interest to reviewers were pain measured by a VAS or a numeric rating scale, and a global assessment measure evaluating overall improvement and/or satisfaction with the intervention.

Outcomes were reported immediately posttreatment (<1 week) and at short-term (1-12 weeks) follow-up. Longer term outcomes (i.e., at 6 and 12 months) were secondary measures. For the pain outcome, meta-analysis of 10 trials found significantly greater reduction in pain scores in the LLLT group at immediate follow-up (WMD = -0.79 cm; 95% CI, -1.22 to 0.36 cm). In a meta-analysis of 6 trials, there was no significant difference in pain reduction at short-term follow-up. However, in subgroup analyses, there was significantly greater reduction in pain with LLLT in trials that used a higher dose (>3 J/point), but not a lower dose, and in trials that included patients with a short duration of back pain (5-27 months) but not long duration (49 months to 13 years). Decisions on the cutoff to use for laser dose and duration of back pain were made post hoc and considered review findings. Findings were similar for the global assessment outcome. Meta-analyses found significantly higher global assessment scores at immediate follow-up (5 trials) but not at short-term follow-up (3 trials). Only 2 trials reported pain or global assessment at 6 months and 12 months and neither found statistically significant differences between the LLLT and sham groups.

In a double-blind RCT, Koldas Dogan et al (2017) compared the effectiveness of 2 laser therapy regimens on pain, lumbar ROM, and functional capacity in patients with chronic low back pain. This trial assessed 49 patients with chronic low back pain who were randomized to a hot pack and the 2 different laser therapies for a total of 15 sessions. A series of assessments were conducted before and after treatment, including a modified Schober test; right and left lateral flexion measurements; VAS; and a modified ODI. After treatment, both groups saw a significant improvement in VAS, ODI, and lumbar ROM ($p<0.05$). However, group 2 saw significantly better results in lateral flexion measurements and ODI scores ($p<0.05$). Trial limitations included: (1) the short duration of follow-up; and (2) use of hot packs, which might have biased the pain measurements. No superiority was found for 1 laser treatment over the other regarding pain relief; however, regarding functionality, patients might find the Helium-Neon laser to be superior.

Section Summary: Low Back Pain

The literature on LLLT for low back pain consists of RCTs and several systematic reviews of RCTs. Meta-analyses found that LLLT resulted in a significantly greater reduction in pain scores and global assessment scores than a placebo control in the immediate posttreatment setting. However, meta-analyses also found that other outcomes (e.g., disability index, ROM) were significantly better immediately after treatment with active versus placebo LLLT and did not find significant benefit of LLLT at longer term follow-up.

Osteoarthritis Knee Pain

Several RCTs and systematic review of RCTs on LLLT for treatment of knee osteoarthritis have been published. In 2015, Huang et al published a systematic review of RCTs comparing at least 8 treatment sessions of LLLT and sham laser treatment in knee osteoarthritis patients. To be eligible for inclusion in the review, trials needed to report pain and/or functional outcomes and a PEDro quality score. A total of nine trials (total N=518 patients) met eligibility criteria. In these studies, the interventions included between eight and 20 laser or sham sessions over 2 to 6 weeks. All 9 trials were considered high quality according to the PEDro scale (score of at least 7 out of 11 possible points). Primary outcomes of interest were post-treatment pain measured by VAS and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores

(pain and function). Meta-analyses did not find that LLLT led to significantly better pain scores than the sham control, either immediately after treatment or at the 3-month follow-up. For example, a meta-analysis of 5 studies that reported 12-week pain scores did not find a statistically significant between-group difference (standardized mean difference [SMD], -0.06; 95% CI, -0.30 to 0.18). Moreover, there were not statistically significant differences between active and sham laser interventions on WOMAC stiffness cores or WOMAC function scores. The secondary outcome, range of motion after therapy, also did not significantly favor LLLT over a sham intervention.

Previously, in 2007, Bjordal et al published a systematic review of placebo-controlled RCTs to determine the short-term efficacy of physical interventions for pain associated with knee osteoarthritis. They included a total of 36 RCTs. The largest proportion of trials evaluated TENS (n=11), followed by eight trials on LLLT and seven on pulsed electromagnetic fields. Also included were trials on electroacupuncture, manual acupuncture, static magnets, and ultrasound. The authors did not report findings of pooled analyses on LLLT for knee osteoarthritis. In a qualitative analysis, they stated that all the physical interventions but two (manual acupuncture, ultrasound) showed better results with active treatment over placebo.

Section Summary: Osteoarthritis Knee Pain

The literature on LLLT for OA includes RCTs and 2 systematic reviews of RCTs. The more recent systematic review, which pooled study findings, did not find that LLLT significantly improved pain and functional outcomes compared with a sham intervention.

Heel Pain

Achilles Tendinopathy

Stergioulas et al randomized 52 recreational athletes with chronic Achilles tendinopathy symptoms to an eight-week (12 sessions) program of eccentric exercises with LLLT or with sham LLLT. By ITT analysis, results for the primary outcome of pain during physical activity on VAS were significantly lower in the exercise group with LLLT group at 4 weeks ($p<0.001$), 8 weeks ($p<0.001$), and 12 weeks ($p=0.007$) after randomization.

Tumilty et al (2012) reported a randomized, double-blinded, sham-controlled trial of LLLT as an adjunct to three months of exercise training in 40 patients with Achilles tendinopathy. Active or sham LLLT was administered 3 times per week for four weeks, and exercises were performed twice a day for 12 weeks. The primary outcome was the Victorian Institute of Sport Assessment–Achilles questionnaire (VISA-A) at 12 weeks. Following treatment, the only significant difference between the groups on an ITT basis was at four weeks on the VISA-A and favored the sham-control group. The VISA-A and numeric rating scale for pain were not significantly different between the active and sham groups at 12-week or 1-year follow-up.

Plantar Fasciitis

A 2015 RCT by Macias et al published a double-blind RCT that 69 patients with unilateral chronic plantar fasciitis and chronic heel pain of three months or longer that was unresponsive to conservative treatments (e.g., rest, stretching, and physical therapy). Patients were randomized to twice weekly treatment for 3 weeks of LLLT or sham treatment. The primary efficacy outcome, difference in reduction of heel pain pre- to post-treatment, differed significantly between groups

($p<0.001$). Mean VAS decreased from 69.1 to 39.5 in the LLLT group and from 67.6 to 62.3 in the sham group. The difference in scores on the Foot Function Index did not differ significantly between groups.

An RCT on LLLT for plantar fasciitis was reported by Kiritsi et al in 2010. The trial was double-blind and sham-controlled trial and included 30 patients. Twenty-five (83%) patients completed the study, with treatment 3 times per week over 6 weeks. At baseline, plantar fascia thickness measured by US was significantly greater in the symptomatic compared with asymptomatic feet (5.3 mm vs 3.0 mm). Plantar fascia thickness decreased in both LLLT and sham groups over the course of the study. Although plantar fascia thickness after 6 weeks of treatment was not significantly different between the 2 groups (3.6 mm LLLT and 4.4 mm sham), there was a significant difference between the groups in the change in thickness (1.7 mm LLLT vs 0.9 mm sham). VAS after night rest or daily activities was significantly improved in the LLLT group compared with the sham, with a 59% improvement in the active laser group and a 26% improvement for the sham-treated subjects. At baseline, pain after daily activities was rated as 67 of 100 by both groups. At the end of treatment, VAS after daily activities was rated as 28 of 100 for LLLT and 50 of 100 for sham.

Cinar et al (2018) conducted a prospective single-blinded RCT investigating combination therapy consisting of LLLT plus exercise and orthotic care vs orthotic care alone in persons with plantar fasciitis. Forty-nine individuals were randomized to LLLT (n=27) or a control therapy (n=22). Each person performed a home exercise routine and received orthotic care; persons in the LLLT group received treatment 3 times a week for a total of 10 sessions. The function subscale of the American Orthopedic Foot and Ankle Society Score, a VAS, and the 12-minute walk test were used to measure progress. Scores were recorded at baseline, 3 weeks, and 3 months after treatment. At week 3, both groups saw a significant improvement in American Orthopedic Foot and Ankle Society total score (LLLT, $p<0.001$; control, $p=.002$). However, at the 3-month follow-up, only the LLLT group progressed as assessed on the American Orthopedic Foot and Ankle Society total score ($p=0.04$). At all check-ins, the group scores for the 12-minute walk test were comparable. Both groups showed significant pain reductions at the 3-month follow-up (LLLT, $p<0.001$; control, $p=0.01$); however, the LLLT group had a more significant reduction in pain at month 3 ($p=0.03$). Thus, reviewers concluded that combination therapy plus LLLT was more effective in reducing pain and improving function for patients with plantar fasciitis than orthotic care alone. Limitations included a lack of a control group, which would have accounted for the natural progression of recovery in patients with plantar fasciitis; another limitation is that the LLLT dose may or may not have been precise enough for the conditions of this study.

Section Summary: Heel Pain

At least 2 sham-controlled randomized trials have evaluated LLLT for heel pain (Achilles tendinopathy, plantar fasciitis) but findings were inconsistent. One RCT compared LLLT plus therapy with orthotic care alone, and while a significant advantage was observed in LLLT treatment, LLLT treatment was used as a combination therapy. None of the studies presented long-term follow-up data. Given all factors, further studies are needed to validate the technology.

Rheumatoid Arthritis
A 2005 Cochrane Review included five placebo-controlled RCTs and found that relative to a separate control group, LLLT reduced pain by 1.10 points on VAS compared with placebo, reduced morning stiffness duration by 27.5 minutes, and increased tip-to-palm flexibility by 1.3 cm. Other outcomes, such as functional assessment, ROM, and local swelling, did not differ between groups. For RA, relative to a control group using the opposite hand (one study), there was no difference observed between the control and treatment hand for morning stiffness duration and no significant improvement in pain relief. The authors noted that "despite some positive findings, this meta-analysis lacked data on how LLLT effectiveness is affected by four important factors: wavelength, treatment duration of LLLT, dosage, and site application over nerves instead of joints."

A 2010 randomized, double-blind, placebo-controlled trial comparing outcomes of pain reduction and improvement in hand function in 82 patients with RA treated with LLLT or placebo laser was reported by Meireles et al. There were no statistically significant differences between groups in most of the outcome measurements including the primary variables, though a few measures significantly favoring either the active or placebo treatment were found. The authors concluded that LLLT at the dosage used in the study was not effective for the treatment of hands among patients with RA.

Section Summary: Rheumatoid Arthritis
A Cochrane review of 5 placebo-controlled RCTs found a significant benefit of LLLT on some outcomes (e.g., VAS) but not others (e.g., functional assessment). A 2010 RCT, published after the Cochrane review, did not find that LLLT was significantly better than a placebo treatment for most outcomes.

Bell Palsy
In 2014, Alayat et al reported on a randomized, double-blind, placebo-controlled trial of laser therapy for the treatment of 48 patients with Bell palsy. Facial exercises and massage were given to all patients. Patients were randomized to one of three groups: high-intensity laser therapy, LLLT, or exercise only. Laser treatment was given 3 times per week to 8 points of the affected side for 6 weeks. At 3 and 6 weeks after treatment, outcomes were assessed using the Facial Disability Scale and the House-Brackmann Scale. Significant improvements in recovery were seen in both laser therapy groups over exercise alone with the most improvement seen with high-intensity laser.

Ordahan and Karahan (2017) investigated the efficacy of LLLT when used in combination with traditional facial exercises to treat facial paralysis. Forty-six patients with Bell palsy were randomized to 2 groups: 1 group underwent LLLT plus facial exercise therapy (FET; n=23); the other group underwent FET alone (n=23). Laser therapy was administered 3 times a week for 6 weeks. Patients were evaluated during the treatment and at 3 and 6 weeks posttreatment. The Facial Disability Index was used to evaluate progress. No significant improvement was observed at week 3 in the FET-alone treatment group ($p<0.05$), but significant improvement was noted at week 6 ($p<0.001$). In the LLLT plus FET group, significant improvement was noted at 3 and 6 weeks ($p<0.001$); moreover, improvements in the Facial Disability Index scores in the LLLT plus FET group were significantly greater than those of the FET-alone treatment group at week 3

and week 6 ($p<0.05$). Study limitation included lack of long-term follow-up and use of combination therapy, which obscures the contribution of LLLT.

Section Summary: Bell Palsy
One RCT found a significant short-term benefit of LLLT over exercise, but long-term outcomes were not available. Another RCT found significant short-term benefit with FET plus LLLT over FET alone, but again, no long-term data were available. The limited evidence on laser therapy for Bell palsy is insufficient to draw conclusions. Because Bell palsy often improves within weeks and may resolve completely within months, it is difficult to isolate specific improvements from laser therapy over the natural resolution of the illness. Also, no sham-controlled trials are available.

Fibromyalgia
In 2007, Matsutani et al randomized 20 patients with fibromyalgia to receive laser treatment and stretching exercises or stretching alone. Outcome measures were VAS and dolorimetry at tender points, QOL on the FIQ, and the 36-Item Short-Form Health Survey (SF-36). At the end of treatment, both groups demonstrated pain reduction, higher pain threshold at tender points (all $p<0.01$), lower mean FIQ scores, and higher SF-36 mean scores (all $p<0.05$). No significant differences were found between groups.

Several small RCTs evaluating LLLT for treating fibromyalgia have been published. In 2014, Ruaro et al reported on 20 patients randomized to receive LLLT or sham treatment three times a week for 4 weeks (total of 12 treatments). Outcomes included scores in the Fibromyalgia Impact Questionnaire (FIQ) which measures physical function, ability to work, pain, fatigue and depression, the McGill Pain Questionnaire (MPQ) and a pain VAS. All 3 outcomes were significantly better in the active compared to sham group after treatment. The mean overall FIQ score was 18.6 in the LLLT group and 5.2 in the sham group ($p=0.003$). Mean change scores also differed significantly between groups for MPQ score ($p=0.008$) and VAS score ($p=0.002$).

Section Summary: Fibromyalgia
Few RCTs evaluating LLLT for treatment of fibromyalgia are available and existing trials are small (i.e., <25 patients each). One RCT with 20 patients found significantly better outcomes with LLLT versus sham and another RCT with 20 patients did not find statistically significant between-group differences on similar outcomes. Additional RCTs with sufficient numbers of patients are needed.

Wound Care and Lymphedema
Clinical Context and Therapy Purpose
The purpose of LLLT in patients who have chronic nonhealing wounds or lymphedema is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of LLLT improve the health outcomes in those who have chronic nonhealing wounds or lymphedema?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is those who have various chronic nonhealing wounds or lymphedema.

Interventions
The therapy being considered is LLLT.

Comparators
The following therapies are currently being used: standard wound care or conservative care (e.g., exercise), compression, and decongestive therapy.

Outcomes
The general outcomes of interest, for wound care, is complete wound healing, and for lymphedema, symptom reduction and functional improvements.

Timing
The effects of LLLT to promote healing or pain relief are expected to occur from weeks to months.

Setting
LLLT is provided in an outpatient setting and may be administered by physical therapists and other practicing alternative medicine.

Chronic Non-healing Wounds
A 2004 evidence report on vacuum-assisted and low-level laser wound therapies for treatment of chronic non-healing wounds prepared for the Agency for Healthcare Research and Quality (AHRQ) was based on 11 studies of LLLT. It stated that "The best available trial [of low-level laser wound therapy] did not show a higher probability of complete healing at 6 weeks with the addition of low-level laser compared to sham laser treatment added to standard care. Study weaknesses were unlikely to have concealed existing effects. Future studies may determine whether different dosing parameters or other laser types may lead to different results.

In 2014 a Cochrane review of RCTs on light therapy, including phototherapy, ultraviolet and laser, for pressure ulcers was published. The few trials available for analysis were of small size and very low quality. The reviewers found the available evidence overall was insufficient to draw conclusion on the effects light therapy on pressure ulcers.

Machado et al (2017) also published a systematic review evaluating the treatment of pressure ulcers with LLLT. Reviewers identified 4 studies meeting eligibility requirements (total N=210 patients). Outcomes were the ulcer area, healing rate, and overall healing rate. Two of the 4 studies used LLLT with a single wavelength; and the other two used LLLT with probe cluster, which employs the simultaneous assimilation of different types of diodes and wavelengths. In the study that employed the 658 nm wavelength, reviewers found that particular frequency reduced pressure ulcers by 71%. The other wavelengths did not produce any significant findings related to the study outcome; moreover, the studies using the probe cluster technique were also not successful in producing significant findings. While studies should be conducted to investigate

further the success found in single wavelength at 658 nm, at this time there is insufficient evidence to suggest LLLT can significantly benefit patients with pressure ulcers.

Section Summary: Chronic Non-healing Wounds
Three systematic reviews of the literature did not find sufficient evidence from controlled studies demonstrating that LLLT is effective for wound healing.

Lymphedema
Several systematic reviews of RCTs and observational studies have been published. In 2015, Smoot et al published a systematic review of studies on the effect of LLLT on symptoms in women with breast cancer–related lymphedema. The authors identified nine studies, seven RCTs and two single-group studies. Three studies had a sham control group, one used a waitlist control, and three compared LLLT to an alternative intervention (e.g., intermittent compression). Only three studies had blinded outcome assessment and, in three studies, participants were blinded. A pooled analysis of four studies found significantly greater reduction in upper-extremity volume with LLLT versus the control condition (effect size [ES], -0.62; 05% CI, -0.97 to - 0.28). Only two studies were suitable for a pooled analysis of the effect of LLLT on pain. This analysis did not find a significant difference in pain between LLLT and control (ES = -1.21; 95% CI, -4.51 to 2.10).

Omar et al published a qualitative systematic review of LLLT for the management of breast cancer-related lymphedema in 2012. They included 8 studies with a total of 230 patients in the review. Five studies were graded as Sackett evidence Level II (small randomized trial with high false-positive or false-negative errors), 2 were graded as Level III (nonrandomized comparative study), and one study was graded as Level V evidence (case series). The authors noted major methodologic flaws and little uniformity in the design of the studies.

One of the larger double-blind RCTs was published in 2011 by Omar et al; the study reported on 50 patients with postmastectomy lymphedema. The average length of time that patients had swelling was 14 months (range, 12-36 month). Patients were treated with active or sham laser three times per week for 12 weeks over the axillary and arm areas. In addition, all participants were instructed to perform daily arm exercises and to wear a pressure garment. Limb circumference, shoulder mobility, and grip strength were measured before treatment and at four, eight, and 12 weeks. Limb circumference declined over time in both groups, with significantly greater reduction in limb circumference in the active laser group at 8 (20.0 vs 16.4 cm), 12 (29 vs 21.8 cm), and 16 weeks (31 vs 23). Shoulder flexion and abduction were significantly better in the active laser group at 8 and 12 weeks. Grip strength was significantly better in the active laser group after 12 weeks of laser therapy (26.2 vs 22.4 kg). The durability of these effects was not assessed.

Section Summary: Lymphedema
Two systematic reviews of RCTs and observational studies found methodologic flaws in the available studies and did not consistently find better outcomes in patients receiving LLLT versus a control condition for treatment of lymphedema.

Summary of Evidence

Oral Mucositis

For individuals who have increased risk of oral mucositis due to some cancer treatments (e.g., chemotherapy, radiotherapy) and/or hematopoietic cell transplantation who receive low-level laser therapy (LLLT), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related morbidity. A 2014 systematic review included 18 RCTs and found better outcomes with LLLT used to prevent oral mucositis than with control treatments. RCTs published after the systematic review had similar findings. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Musculoskeletal and Neurologic Disorders

For individuals who have carpal tunnel syndrome who receive LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Both a 2016 systematic review and a 2010 TEC Assessment did not find sufficient evidence from RCTs that LLLT improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have neck pain who receive LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A 2013 systematic review identified 17 trials, most of which were considered low quality. Only 2 trials were considered moderate quality and they found that LLLT led to better outcomes than placebo for chronic neck pain. A 2010 TEC Assessment found conflicting evidence. Additionally, laser types, application dosages, and treatment schedules vary in the available evidence and require further study. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have subacromial impingement syndrome who receive LLLT, the evidence includes RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Most trials did not show a significant benefit of LLLT compared with sham treatment or with an alternative intervention (e.g., exercise). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have adhesive capsulitis who receive LLLT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A Cochrane review on treatments for adhesive capsulitis identified 2 RCTs assessing LLLT. Due to the small number of trials and study limitations, reviewers concluded that the evidence was insufficient to permit conclusions about the effectiveness of LLLT for adhesive capsulitis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have temporomandibular joint pain who receive LLLT, the evidence includes RCTs and several systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Meta-analyses of RCTs had mixed findings. A 2015 meta-analysis, which included 14 placebo-controlled RCTs, did not find a statistically significant impact of LLLT on pain, but did find that LLLT significantly improved

functional outcomes (e.g., mouth opening). RCTs have not compared the impact of LLLT with physical therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have low back pain who receive LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Meta-analyses of RCTs found that LLLT resulted in a significantly greater reduction in pain scores and global assessment scores than a placebo control in the immediate posttreatment setting. Meta-analyses also found that other outcomes (e.g., disability index, range of motion) were significantly better immediately after treatment with active rather than placebo LLLT, but not at longer term follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have osteoarthritic knee pain who receive low LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A 2015 systematic review, which pooled study findings, did not find that LLLT significantly improved pain or functional outcomes compared with a sham intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heel pain (i.e., Achilles tendinopathy, plantar fasciitis) who receive LLLT, the evidence includes RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Findings of 2 sham-controlled randomized trials were inconsistent, and while an RCT compared LLLT with standard care lacked long-term follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have rheumatoid arthritis who receive low LLLT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A systematic review of RCTs found inconsistent benefit of LLLT for a range of outcomes. A 2010 RCT, published after the systematic review, did not find that LLLT was significantly better than a placebo treatment on most outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Bell palsy who receive LLLT, the evidence includes two RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT found significant short-term benefit of LLLT over exercise. Longer term outcomes beyond 6 weeks were not available. Because Bell palsy often improves within weeks and may completely resolve within months, it is difficult to isolate specific improvements from laser therapy over the natural resolution of the illness. In addition, no sham-controlled trials are available. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have fibromyalgia who receive LLLT, the evidence includes RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCTs evaluating LLLT for treatment of fibromyalgia are small (i.e., <25 patients

each). One RCT (N=20 patients) found significantly better outcomes with LLLT than with sham, while another (N=20 patients) did not find statistically significant between-group differences for similar outcomes. Additional RCTs with sufficient numbers of patients are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Wound Care and Lymphedema

For individuals who have chronic non-healing wounds who receive LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The few existing RCTs tend to have small sample sizes and potential risk of bias. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have lymphedema who receive LLLT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Two systematic reviews found methodologic flaws in the available studies and did not consistently find better outcomes for patients receiving LLLT than receiving a control condition for treatment of lymphedema. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

Mucositis Prevention Guideline Development Group

In 2017, the Mucositis Prevention Guideline Development Group published guidelines on preventing oral and oropharyngeal mucositis in children undergoing hematopoietic cell transplantation. The guidelines were based on an evidence review consisting of randomized controlled trials that evaluated interventions such as cryotherapy and low-level laser therapy (LLLT). The guidelines suggested that LLLT could be offered to children but classified this recommendation as weak.

Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology

In 2014, the Mucositis Guidelines leadership Group of the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) published a guideline on the management of mucositis secondary to cancer therapy.

For the prevention of oral mucositis, the MASCC/ISOO recommended the following treatments, based on strong evidence: LLLT (650 nm, power of 40 mW) in patients receiving HSCT conditioned with high-dose chemotherapy with or without total body irradiation; oral cryotherapy in patients receiving bolus 5- fluorouracil chemotherapy; recombinant human keratinocyte growth factor-1 in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous stem cell transplantation for a hematological malignancy; benzydamine mouthwash in patients with head and neck cancer receiving moderate dose radiotherapy without concomitant chemotherapy.

Additionally, the following treatments were recommended for the prevention of oral mucositis based on weaker evidence: LLLT (~632.8nm) in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer; oral care protocols for patients undergoing

any cancer treatment; oral cryotherapy in patients receiving high-dose melphalan as conditioning for HSCT; oral zinc supplements in oral cancer patients receiving radiotherapy or chemoradiation.

American Physical Therapy Association

The American Physical Therapy Association (2010) published guidelines on the diagnosis and treatment of Achilles tendinitis. LLLT received a level B recommendation (based on moderate evidence) for decreasing pain and stiffness in patients with Achilles tendinopathy. The guidelines concluded that "given the limited number of studies employing LLLT in this population, additional study is warranted." In 2014, the Association stated in a press release, based on a Cochrane review, that "It could be that low-level laser therapy (LLLT) is a useful electrotherapy modality for treatment of adhesive capsulitis, but the effects are marginal, and evidence is a long way from conclusive…."

National Institute for Health and Clinical Excellence

The U.K.'s National Institute for Health and Clinical Excellence 2009 Guideline on early management of persistent nonspecific low back pain did not recommend laser treatment, citing limited evidence. The 2016 updated guidance does not mention laser therapy. In 2018, the Institute released guidance stating that it was considering LLLT and that it would issue and interventional procedures consultation document regarding the safety and efficacy of the treatment; at the time of this writing, the Institute was still in progress of releasing their disclosure.

American Pain Society

The 2007 American Pain Society guideline states that there is insufficient evidence to recommend LLLT for treatment of low back pain, and LLLT is not mentioned in the 2009 guideline. The American College of Physicians (2017) released guidelines relating to noninvasive treatments for chronic low back pain. The guidelines strongly recommended that patients with chronic low back pain should first seek nonpharmacologic treatment such as exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction-all based on moderate quality evidence. The recommendation also stated that patients with chronic low back pain should seek treatments such as tai chi, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, LLLT, operant therapy, cognitive behavioral therapy, or spinal manipulation-all based on low-quality evidence. While the College stated that LLLT has a small effect on pain and function, it found the evidence insufficient for the use of LLLT.

American Academy of Orthopaedic Surgeons

The American Academy of Orthopaedic Surgeons' 2016 guidelines on management of carpal tunnel syndrome rated laser therapy state: "limited evidence". The guidelines state "limited evidence supports that laser therapy might be effective compared to placebo."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Key Words:
Low-level laser therapy (LLLT), laser therapy, cold laser, cold laser therapy, class III laser, Micro Light laser, photobiomodulation, high power laser therapy (HPLT), class IV high power laser, MLS laser therapy, Cutting Edge MLS M6 Robotic Laser, Avicenna's laser, GRT LITE, Excalibur IV Laser, Acculaser Pro, Tuco Erchonia PL3000, Light Stream low level laser.

Approved by Governing Bodies:
A number of low-level lasers have received clearance for marketing from the U.S. Food and Drug Administration (FDA) for the treatment of pain.

Data submitted to the FDA as part of the FDA 510(k) approval process for the MicroLight 830® Laser consisted of application of the laser over the carpal tunnel three times a week for five weeks. The labeling states that the "MicroLight 830 Laser is indicated for adjunctive used in the temporary relief of hand and wrist pain associated with Carpal Tunnel Syndrome."

In 2006, the FDA provided marketing clearance for the GRT LITE™, which listed the Tuco Erchonia PL3000, the Excalibur System, the Microlight 830 Laser, and the Acculaser Pro as predicate devices. Indications of the GRT LITE for carpal tunnel syndrome are similar to the predicate devices: "adjunctive use in providing temporary relief of minor chronic pain."

The LightStream™ Low Level Laser device received 510(k) marketing clearance in 2009 for adjunctive use in the temporary relief of pain associated with knee disorders with standard chiropractic practice. A number of clinical trials of LLLT are underway in the United States, including studies of wound healing.

Since 2009, many more similar LLT devices have received 510(k) clearance from FDA; most recently, in 2018, Super Pulsed Laser technology (Multi Radiance Medical) was approved by FDA through the premarket approval process for use in neck and shoulder pain.

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:
CPT Codes:

97026	Application of a modality to one or more area; infrared
97039	Unlisted modality (specify type and time if constant attendance)
97139	Unlisted therapeutic procedure

HCPCS	**S8948**	Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes

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Policy History:

Medical Policy Group, May 2006 **(3)**
Medical Policy Administration Committee, June 2006
Available for comment July 5-August 18, 2006
Medical Policy Group, February 2007 **(3)**
Medical Policy Administration Committee, February 2007
Available for comment February 10-March 26, 2007
Medical Policy Group, March 2009 **(4)**
Medical Policy Administration Committee, April 2009
Available for comment March 18-May 1, 2009
Medical Policy Group, January 2010 **(3)**
Medical Policy Group, October 2010 **(3)**
Medical Policy Group, January 2010
Medical Policy Group, March 2011 **(3)**
Medical Policy Administration Committee March 2011
Available for comment April 4 – May 18, 2011
Medical Policy Group, December 2011 **(3)**: Updated investigational list under Policy section, and updated Key Points, & References

Medical Policy Group, December 2012 **(3)**: 2012 Updates to Description, Policy (added more indications), Key Points, and References
Medical Policy Administration Committee, January 2013
Available for comment December 12, 2012 through January 26, 2013
Medical Policy Panel, November 2013
Medical Policy Group, January 2014 **(2):** Policy statement unchanged. Description, Key Points, References updated with findings of literature review through September 2013. Outdated web references deleted.
Medical Policy Panel, November 2014
Medical Policy Group, November 2014 **(4):** No policy change. Updates to Key Points and References
Medical Policy Group, January 2015 (**6**): Ad hoc review with update to Key Words to include Cutting Edge MLS M6 Robotic laser, no change to policy statement.
Medical Policy Panel, February 2016
Medical Policy Group, February 2016 **(6):** Updates to Description, Key Points, Practice Guidelines and Position Statements, and References; no change to policy statement.
Medical Policy Panel, February 2017
Medical Policy Group, March 2017 **(6)**: Updates to Description, Key Points, Practice Guidelines, Coding and References. No change to policy intent.
Medical Policy Panel, July 2018
Medical Policy Group, July 2018 **(6)**: Updates to Key Points, Practice Guidelines and References.
