


<b>MEDICAL POLICY</b>	<b>Low-Level and High-Power Laser Therapy</b>
<b>Effective Date: 10/1/2021</b>	Medical Policy Number: 201
 <div style="text-align: right;">10/1/2021</div>	Technology Assessment Committee Approved Date: 4/10; 7/12; 8/13; 7/14; 7/15; 4/16:
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Medical Officer	Date

**See Policy CPT/HCPCS CODE section below for any prior authorization requirements**

**SCOPE:**

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**

All lines of business

**BENEFIT APPLICATION**

Medicaid Members

*Oregon:* Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

**POLICY CRITERIA**

- I. Low-level laser therapy for the prevention of oral mucositis may be considered **medically necessary and covered** for members undergoing cancer treatment associated with increased risk or oral mucositis, including chemotherapy, radiotherapy, and/or hematopoietic stem cell transplantation.
- II. Low-level laser therapy (i.e., cold laser therapy) and high-power laser therapy (i.e., class IV laser) are considered **investigational and not covered** when criterion I. is not met. Investigational indications include, but are not limited to, the following (A- G.):
  - A. Treatment of oral mucositis
  - B. Carpal tunnel syndrome
  - C. Hair loss
  - D. Low back pain

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<ul style="list-style-type: none"> <li>E. Rotator cuff tendinopathy</li> <li>F. Pressure ulcers</li> <li>G. Chronic pain</li> </ul> <p>Link to <a href="#">Policy Summary</a></p>
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## BILLING GUIDELINES

CPT code 0552T will be covered if billed with one of the following diagnosis codes:

- C00.0 – C17.9
- C22.0 – C96.9
- K12.30 – K12.39

0552T will be denied as investigational if billed with any other diagnosis codes.

## CPT/HCPCS CODES

All Lines of Business	
No Prior Authorization Required	
0552T	Low-level laser therapy, dynamic photonic and dynamic thermokinetic energies, provided by a physician or other qualified health care professional
Not Covered	
S8948	Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes
<p>Unlisted Codes</p> <p>All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then it will be denied as <b>Not Covered</b>.</p>	
97039	Unlisted modality (specify type and time if constant attendance)
97799	Unlisted physical medicine/rehabilitation service or procedure

## DESCRIPTION

### Low-Level Laser Therapy (LLTT)

According to Hayes, “LLLT is a noninvasive treatment that involves the application of light from a low-intensity laser at a wavelength of 633, 670, 830, 860, or 904 nanometers.”<sup>1</sup> This treatment can be done in the physician’s office and requires no sedation or anesthesia. LLLT involves the application of laser

light to various acupuncture points for several seconds, depending on the intensity of the laser. The biomechanical mechanism of LLLT remains unclear; however, “LLLT may improve pain and induce healing by a biostimulatory effect following absorption of the light.”<sup>1</sup>

#### High-Power Laser Therapy (HPLT)

High-power, or class IV, lasers, “produce rapid increases in superficial tissue temperatures when maximum permissible exposure limits are exceeded.”<sup>2</sup> Compared to low-level lasers, these lasers are able to transmit energy beyond skin deep to the musculoskeletal tissues. “High-power lasers have been used to treat the pain associated with acute and chronic musculoskeletal disorders and may promote tissue repair by increasing blood flow.”<sup>2</sup>

## REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of low-level laser therapy and high-power laser therapy. Below is a summary of the available evidence identified through May 2021.

#### Low-Level Laser Therapy

##### *Carpal Tunnel Syndrome*

- In 2016 (archived in 2021), Hayes conducted an evidence review of low-level laser therapy (LLLT) as a treatment for patients with mild to moderate carpal tunnel syndrome (CTS).<sup>1</sup> The review included 11 RCTs, with sample sizes ranging from 45 to 100. Follow-up times averaged 3 months. Six of the included RCTs evaluated LLLT compared to sham laser treatment, while another six evaluated LLLT compared to active controls (e.g. ultrasound, splinting, or steroid injections either alone or concurrently to another conservative treatment). The primary outcomes of interest were pain and functionality as assessed by the pain visual analog scale (VAS), symptom severity score (SSS), functional status score (FSS), pinch strength and grip strength.

The results of the RCTs were conflicting across all outcomes, with all RCTs reporting improvements from baseline in almost all groups (i.e. treatment groups, active control groups and sham groups). Hayes rated the body’s overall quality of evidence as “low,” largely due to these unexplained inconsistencies across studies. The validity of results was further limited by inadequate follow-up, a lack of power analyses, small sample sizes, and a lack of blinding of patients and/or outcome assessors. Hayes assigned a “C” rating (potential but unproven benefit) for the use of LLLT for treatment of mild to moderate CTS, reflecting low-quality and inconsistent evidence. Hayes concluded that “substantial uncertainty remains regarding the extent of treatment benefit in comparison with other treatment modalities, long-term health benefits, safety, and patient selection criteria.”<sup>1</sup>

- In 2017, Rankin et al. conducted a Cochrane systematic review and meta-analysis to evaluate low-level laser therapy (LLLT) for carpal tunnel syndrome (CTS).<sup>3</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Study authors were also contacted, if necessary, for additional information or data. The primary outcomes of interest were short term ( $\leq 3$  months) symptom severity score, functional status, and visual analogue scale (VAS) pain. Secondary outcomes of interest included other musculoskeletal functional assessments, such as grip strength and finger-pinch strength.

Authors identified 22 randomized controlled trials as eligible for inclusion (n=1153). Risk of bias varied, but was high or unclear in a majority of the included studies. Due to several methodological limitations, the quality of evidence was rated as very low or low for most studies. At short term follow-up ( $\leq 3$  months), there was very low-quality evidence for any effect over placebo for LLLT on CTS for symptom severity score or functional status. Due to very low quality evidence, the results were inconclusive as to whether LLLT resulted in greater improvement in placebo for the VAS pain and several other secondary outcome measures. When compared with placebo, study results suggested LLLT may slightly improve grip strength and finger-pinch strength; however, this was based on a low quality body of evidence.

Strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers, large sample size, and assessment of heterogeneity. Limitations were identified in the poor quality of included studies, potential for biases, and significant heterogeneity between studies. The authors concluded, “(t)here is insufficient evidence to support LLLT being better or worse than any other type of non-surgical treatment in the management of CTS. Any further research of LLLT should be definitive, blinded, and of high quality.”<sup>3</sup>

- In 2020, Cheung and colleagues published a systematic review and meta-analysis on LLLT for CTS.<sup>4</sup> The review included 6 randomized controlled trials, totalling 418 patients. The analysis compared LLLT plus splinting, sham laser plus splinting, ultrasound plus splinting, and splinting alone and found that LLLT plus splinting had the highest probability of pain reduction at 75%, but that difference was not clinically significant compared to sham. LLLT plus splinting did not significantly improve symptom severity and functional status compared to splinting alone. The authors concluded, “The use of LLLT in addition to splinting for the management of CTS is not recommended, as LLLT offers limited additional benefits over splinting alone in terms of pain reduction, reduction of symptom severity or improved functional status.”

### *Hair Loss*

#### Systematic Reviews

- In 2019, Liu and colleagues conducted a systematic review and meta-analysis evaluating the comparative effectiveness of low-level laser therapy for adult androgenic alopecia (AGA).<sup>5</sup> Independent investigators systematically searched the literature through October 2018, identified eligible studies, assessed study quality, extracted data and pooled results. In total, 8 studies comprising a total of 11 double-blinded RCTs were included for review. The primary outcome of interest was the standardized mean differences (SMD) of hair density between the LLLT and sham

groups. A positive SMD value indicates LLLT is a more favorable treatment option comparing to sham. A random effects model was employed to pool individual SMDs. Meta-analysis showed a significant increase in hair density for those treated by LLLT versus sham group (SMD 1.316, 95% confidence interval, CI 0.993 to 1.639). The subgroup analysis demonstrated that LLLT increases hair growth in both genders, in both comb- and helmet-type devices, and in short- and long-term treatment course. The subgroup analysis also showed a more significant increase of hair growth for the LLLT versus sham in the low-frequency treatment group (SMD 1.555, 95% CI 1.132 to 1.978) than in the high-frequency group (SMD 0.949, 95% CI 0.644 to 1.253). Investigators concluded that LLLT represents a potentially effective treatment for AGA. Limitations included the heterogeneity of studies included for review, as well as studies' small sample sizes, lack of adequate follow-up and varying treatment parameters.

- In 2017, Afifi and colleagues conducted a systematic review of the evidence for low-level laser therapy (LLLT) in the treatment of hair loss.<sup>6</sup> Independent reviewers systematically identified eligible studies, assessed quality and extracted data for articles published through November 2015. Eleven studies (n=680) met pre-defined criteria and were included for review (1 case report, 1 case series, 4 cohort studies and 5 RCTs). Follow-up times varied between 2 and 24 months. Nine of the 11 studies included for review reported significant improvements in hair count and hair density, and 2 of 4 studies reported significant improvements in hair thickness and tensile strength. No serious adverse events were reported. Limitations of the study include the small sample sizes of studies included for review and heterogeneity among patient populations and study design (e.g. differences in devices used, irradiation parameters, treatment doses, length of treatment, treatment frequencies, and assessment tools). Additionally, 4 out of the 5 RCTs included for review were industry-funded, introducing another possible source of bias. Investigators stated that treatment protocol currently lacks standardization and concluded that "future large sample RCT studies should be, if possible, conducted without any conflicts of interest to further minimize any source of bias."<sup>6</sup>
- In 2017, Gupta et al. conducted a systematic review of the evidence for low-level laser therapy (LLLT) in the treatment of hair loss.<sup>7</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. The primary outcome of interest was change in hair density (per cm<sup>2</sup>). The secondary outcome of interest was patient satisfaction, including overall improvement in hair thickness/fullness of hair. The authors identified 9 studies (5 randomized controlled trials, 1 retrospective observational study, and 3 case series) as eligible for inclusion. Of the 9 studies, 5 evaluated the comb LLLT system (n=461) and 4 evaluated the helmet/cap LLLT system (n=133). All studies reported improvement in hair density at 16 to 26 weeks follow-up with LLLT compared to the sham devices; however, the authors determined evidence to be insufficient to make any sound conclusions regarding LLLT for hair loss. The authors stated that "(d)ata comparison across LLLT trials and with traditional hair loss therapy (minoxidil, finasteride) was not straight forward because there was a lack of visual evidence, sample sizes were low, and there were large variations in study duration and efficacy measurements."<sup>7</sup>

Methodological strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers. Significant limitations are present in the poor methodological quality of selected studies and the small number of selected studies (potential publication bias). Ultimately, the authors concluded "(t)here are a number of unanswered

questions about the optimum treatment regimen, including maintenance treatment and the long-term consequences of LLLT use.”<sup>7</sup>

### Randomized Controlled Trials

Several recent RCTs evaluating the use of low-level laser therapy (LLLT) for the treatment of hair loss were also identified.<sup>8-11</sup> Although studies reported positive results, generalizability is limited due to diverse treatment protocols between studies, small sample sizes (n= 10-100) and inadequate follow-up (4 to 6 months). Two systematic reviews<sup>12,13</sup> recently endorsed LLLT on the basis of studies also evaluated by Afifi et al (2017),<sup>6</sup> discussed above.

### *Low-Back Pain*

- In 2018, the Agency for Healthcare Research and Quality (AHRQ) published a systematic review of RCTs evaluating noninvasive non-pharmacological treatments for five common chronic pain conditions, including chronic low back pain (LBP).<sup>14</sup> Control groups were treated either with usual care, no treatment, placebo or sham intervention, pharmacological therapy, or exercise. Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Three studies evaluating LLLT for the treatment of LBP met pre-defined inclusion criteria and were individually assessed. Included studies reported positive associations between LLLT and LBP, compared to control groups, in short-term function (2 trials, pooled difference -14.98, 95% CI -23.88 to -6.07, I<sup>2</sup> =39%, 0-100 scale); short-term pain (3 trials, pooled difference -1.81, 95% CI -3.35 to -0.27, I<sup>2</sup> =75%, 0-10 scale); and quality of life (MD 4.5, 95% CI 0.7 to 8.2). Despite improvements in the short term (i.e. 1 to 6 months follow-up), investigators found no clear improvement in function at the intermediate or long term follow-up. The overall evidence quality was assessed as “low” among included trials, stemming from unclear allocation concealment methods, high attrition, and inadequate follow-up (less than 1 year).
- In 2016, Glazov and colleagues conducted a systematic review and meta-analysis to evaluate low-level laser therapy (LLLT) for chronic non-specific low back pain.<sup>15</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Study authors were also contacted, if necessary, for additional information or data. The primary outcomes of interest were pain and global assessment of improvement with short-term follow-up. Secondary outcomes of interest were disability, range of back movement, and adverse effects. The authors identified 15 randomized controlled trials as eligible for inclusion; thus producing a sample size of 1,039 participants. A total of three included trials were determined to be at “high risk of bias”. The results of the meta-analysis indicated a statistically significant reduction in total pain scores in laser versus control groups at immediate follow-up. At short-term follow-up, there were no statistically significant differences and substantial heterogeneity between studies was observed. The meta-analysis results also showed a significant effect on global assessment in favor of laser therapy at immediate follow-up; however, no significant difference was observed at the short-term follow-up.

Methodological strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers, large sample size, and assessment of heterogeneity. Significant limitations were present due to the poor

quality of many included studies, inadequate data reporting by many studies, and significant inter-study heterogeneity. Although the results indicated an immediate benefit of laser therapy, the authors concluded, “(r)igorously blinded trials using appropriate laser dosage would provide greater certainty around this conclusion.”<sup>15</sup>

### Randomized Controlled Trials

Several recent RCTs<sup>16-18</sup> not included in the AHRQ review above<sup>14</sup> reported mixed results for low-level laser therapy for the treatment of low-back pain. Generalizability was further limited by diverse treatment protocols between studies, small sample sizes (n= 49 to 100) and inadequate follow-up (3 weeks to 6 months).

### *Rotator Cuff Tendinopathy*

- In 2016, Boudreault et al. conducted a systematic review and meta-analysis to evaluate the efficacy of laser therapy (LT) for rotator cuff (RC) tendinopathy.<sup>19</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. The outcomes of interest included patient reported outcomes such as pain, function, health-related quality of life, as well as performance-based outcomes such as shoulder range of motion (ROM) and muscle strength.

Following systematic review, the authors identified 13 randomized controlled trials as eligible for inclusion. “All included studies compared the effectiveness of LT either alone or in combination with other modalities to various interventions such as oral non-steroidal anti-inflammatory drugs (NSAIDs), exercise, ultrasound, or a placebo.”<sup>19</sup> When comparing LT to clinical recommendation alone, a statistically significant difference was observed between groups in favor of LT. A statistically significant difference was also observed when comparing LT to placebo (sham LT) and ultrasound therapy. However, the results also indicated that (1) LT was not superior to an exercise program and (2) LT in conjunction with exercise was not superior to exercise alone. The evidence for self-reported function and shoulder ROM was inconclusive.

Methodological strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers. Significant limitations are present in the poor methodological quality of selected studies, small number of selected studies (potential publication bias), and not assessing heterogeneity before conducting meta-analyses. The authors concluded, “low to moderate grade evidence supports that LT may reduce pain in the short term in adults with RC tendinopathy, while its effects on function and ROM are not supported.”<sup>19</sup> However, authors also stated, “until more high quality evidence demonstrates clearly the efficacy of LT, clinicians should use LT cautiously.”<sup>19</sup>

### *Pressure Ulcers*

- In 2017, Machado and colleagues published a systematic review of RCTs evaluating low-level laser therapy (LLLT) for the treatment of pressure ulcers (PU).<sup>20</sup> Searching the literature through May 2016, independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Sample sizes in included studies ranged from 18 to 86. Outcomes of interest were ulcer area, healing rate and overall healing rate. In total, 4 RCTs were included for review, 2

evaluating the use of LLLT with single wavelength and 2 evaluated LLLT used to probe the cluster. The former 2 studies reported a statistically significant 71% reduction of the pressure ulcer, with 47% of patients experiencing complete healing at one-month follow-up. The 2 studies evaluating LLLT to probe the cluster reported no significant difference between treatment and control groups.

Investigators noted that a definitive determination of treatment efficacy was not possible given the, small number of studies, their small sample sizes and differing treatment parameters. Investigators concluded that “there is insufficient evidence to ensure the effectiveness of the LLLT treatment on PU, and studies with higher methodological quality should be performed using parameters similar to those which have found significant results in this review.”<sup>20</sup>

In 2014, Chen and colleagues conducted a Cochrane systematic review and meta-analysis to evaluate phototherapy (e.g., light or laser therapy) for treating pressure ulcers.<sup>21</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Study authors were also contacted, if necessary, for additional information or data. The outcomes of interest included time to complete healing (weeks), proportions/numbers of ulcers healed, and adverse events. The authors identified 7 randomized controlled trials (n=403) as eligible for inclusion. All of the included trials were determined to have an unclear risk of bias. “Overall, there was insufficient evidence to determine the relative effects of phototherapy for healing pressure ulcers.”<sup>21</sup> Time to complete healing for laser therapy was evaluated in one RCT, and the results indicated the laser group had a longer mean time to complete healing than the control group. The authors were unable to pool data to evaluate the proportions/numbers of ulcers healed due to between-study variations in outcome measures and treatment durations. In regards to adverse events, no statistically significant difference between groups was identified.

Strengths of this systematic review include the gathering of evidence, assessment of quality, and extraction of data by several independent reviewers following the Cochrane methodology. However, methodological limitations are present in the poor quality of included studies, the small number of included studies, the small sample size, and the inability to conduct meta-analyses due to significant between-study heterogeneity. The authors concluded “(w)e are very uncertain as to the effects of phototherapy in treating pressure ulcers. The quality of evidence is very low due to the unclear risk of bias and small number of trials available for analysis. The possibility of benefit or harm of this treatment cannot be ruled out. Further research is recommended.”<sup>21</sup>

### *Oral Mucositis*

#### Systematic Reviews

- In 2020, Peng and colleagues published a systematic review and meta-analysis on the prevention and treatment of oral mucositis (OM).<sup>22</sup> Thirty randomized studies were included in the analysis, totalling 1616 participants. Twenty-six studies investigated prophylactic LLLT, and 6 studies reported on therapeutic LLLT treatment. Of the 30 studies, 19 were found to be high quality and 11 were low quality. Prophylactic LLLT significantly reduced the overall risk of severe OM (RR= 0.40; 95% CI: 0.28–0.57; P < .01). Prophylactic LLLT also reduced the overall mean grade of OM, overall incidence of severe pain, mean score of pain, and incidence of severe OM, at the most anticipated time. Therapeutic LLLT did not significantly decrease the number of patients with severe OM after 7-day treatment (P= 0.14) compared to the control group, but significantly reduce duration of severe OM



by 5.81 days ( $P < .01$ ). Limitations of the analysis include some heterogeneity between studies, 11 studies with high-risk of bias, with lack of blinding in the majority of studies. For therapeutic LLLT, only 3 studies ( $n=143$ ) were included in the analysis. The authors conclude that prophylactic LLLT is effective in preventing OM in patients receiving chemotherapy and radiotherapy, and therapeutic LLLT is effective in reducing severe OM duration. They suggest that more well-designed multicenter RCTs are needed to assess different laser parameters and LLLT schedules.

- In 2020, De Lima and colleagues conducted a systematic review and meta-analysis assessing the effectiveness of low-level laser therapy for oral mucositis prevention in patients undergoing chemoradiotherapy for the treatment of head and neck cancer.<sup>23</sup> Independent investigators systematically searched the literature through May 2019, identified eligible studies, assessed study quality, extracted data and pooled data. In total, 4 studies were included in the review and 3 studies were included for meta-analysis ( $n=500$ ). The primary outcome of interest was the incidence of oral mucositis. Meta-analysis showed that laser therapy prevents oral mucositis incidence in 28% and 23% of cases at 3 and 4 weeks' follow-up, respectively, in comparison to a placebo-treated control group. Results also indicated that laser therapy was effective in preventing oral mucositis from the 15th to the 45th days of chemoradiotherapy, although LLLT was not effective in preventing pain incidence. All studies were assessed as being at moderate risk of bias. Authors called for additional, high-quality studies to further validate findings and establish patient selection criteria.
- In 2019, Anschau and colleagues conducted a systematic review and meta-analysis evaluating the efficacy of low-level laser for the treatment of cancer oral mucositis (OM).<sup>24</sup> Independent investigators systematically searched the literature through October 2018, identified eligible studies, assessed study quality, extracted data and pooled results. In total, 5 RCTs assessing 315 patients were included for review. The primary outcome of interest was the treatment's effect on OM severity, assessed as a dichotomous variable (e.g. improvement or no improvement in severe OM at 1-week follow-up). Findings showed LLLT to be effective, conferring a 62% risk reduction of severe OM at 1-week follow-up ( $RR = 0.38$  [95% CI, 0.19-0.75]). Investigators concluded that moderate evidence supports LLLT as effective in resolving OM lesions in adult patients undergoing cancer therapy, potentially decreasing the resolution time of OM lesions by approximately 4.21 days. Limitations included heterogeneity of treatment protocols among studies included for review, risk of allocation bias, and the lack of high-quality RCTs conducted to date.

In 2018, He and colleagues published a systematic review and meta-analysis evaluating the use of low-level laser therapy (LLLT) in the treatment of chemotherapy-induced oral mucositis in pediatric and young patients.<sup>25</sup> Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. The outcomes of interest were the effect of LLLT on the prevention or treatment of oral mucositis, as determined by incidence, severity, duration in days, and pain intensity. After screening 219 publications according to pre-defined criteria, investigators included 8 studies for review ( $n=373$ ). Two studies were non-randomized controlled trials, and 6 were RCTs. Included studies were conducted in Brazil ( $n=5$ ), Italy ( $n=2$ ) and Iran ( $n=1$ ). Investigators reported that the odds ratio for developing oral mucositis was significantly lower among patients treated with prophylactic LLLT compared with patients receiving placebo ( $OR = 0.50$ , 95% CI 0.29 to 0.87,  $p = 0.01$ ). Moreover, among LLLT patients, the odds ratio for developing grade III oral mucositis or worse was significantly lower compared with patients treated with placebo ( $OR = 0.30$ , 95% CI (0.10, 0.90),  $p = 0.03$ ), as was the severity of oral mucositis ( $SMD = -0.56$ , 95% CI (-0.98, -0.14),  $p =$

0.009). Compared to routine care, patients receiving therapeutic LLLT experienced reductions in oral mucositis severity (SMD= -1.18, 95% CI (-1.52, -0.84),  $p < 0.00001$ ), and oral pain (MD = - 0.73, 95% CI (- 1.36, - 0.11),  $p = 0.02$ ).

Strengths of this study include the systematic review of literature following a pre-defined protocol and evaluation of methodological quality by independent reviewers. Strength was also found in the assessment of heterogeneity to determine the appropriateness of conducting a meta-analysis. Limitations for this systematic review include the low quality of several studies included for review, the small number of RCTs available for meta-analysis, the small sample size of several included trials, and the lack of trials conducted outside of low-middle income treatment settings. Investigators concluded that “further research should investigate the optimal parameter of LLLT in pediatric and young patients, and studies with higher methodological quality should be performed.”<sup>25</sup>

- In 2014, Oberoi and colleagues conducted a systematic review and meta-analysis of 18 RCTs (n=1,133) evaluating low-level laser therapy (LLLT) for the treatment of oral mucositis.<sup>26</sup> Of the 18 RCTs, 8 studies evaluated patients undergoing hematopoietic stem cell transplantation (HSCT); 8 evaluated head and neck cancer patients receiving radiotherapy or chemoradiation; and 2 evaluated patients with other conditions receiving chemotherapy. Independent reviewers systematically identified eligible studies, assessed quality, extracted data, and employed the Cochrane risk of bias tool to evaluate findings. The primary outcome of interest was the incidence of severe mucositis in children and adults with cancer or undergoing HSCT compared to placebo or no therapy. Secondary outcomes included: overall mean grade of mucositis; duration of severe mucositis; incidence of any pain and severe pain; and overall mean pain scores. Across ten studies (n=689), the overall incidence of severe mucositis (grades 3-4) decreased with prophylactic LLLT when compared to patients receiving placebo or no therapy (RR 0.37 (95% CI 0.20 to 0.67,  $p = 0.001$ ). Absolute risk reduction in the incidence of severe mucositis was -0.35 (95% CI -0.48 to -0.21,  $p < 0.001$ ). Six studies (n=546) were used to measure secondary outcomes. LLLT significantly reduced the overall mean grade of mucositis (standardized mean difference [SMD], -1.49; 95% CI, -2.02 to -0.95), duration of severe mucositis (WMD -5.32, 95% CI -9.45 to -1.19), and incidence of severe pain (VAS; RR=0.26, 95% CI 0.18 to 0.37). Investigators found no significant relationship between the type of condition treated and the efficacy of LLLT.

Strengths of this study include the systematic review of literature following a pre-defined protocol and evaluation of methodological quality by two independent reviewers. However, only four studies included for review were at low risk of bias. There was also heterogeneity across studies with respect to laser parameters, laser schedules, mucositis assessment scales, time point of assessments and outcome reporting. Investigators concluded that “future research should identify the optimal characteristics of LLLT and determine feasibility in the clinical setting.”<sup>26</sup>

#### Randomized Controlled Trials

- In 2012, Gautam and colleagues published results from their RCT evaluating low-level laser therapy (LLLT) for prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.<sup>27</sup> Fifty-five patients received LLLT before radiotherapy at 66 Gy delivered daily in 33 fractions, five days per week, concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm<sup>2</sup>, and a dosage of 3 to 3.5 J. Patients in the control group (n=55) received sham treatment prior to radiation for 6.5 weeks. Pain and total parenteral nutrition (TPN) were

measured weekly by blinded assessors. Descriptive statistics, t-test and Man Whitney U test were used to analyzed data. Patients who received LLLT before radiotherapy experienced significant reductions in the incidence of severe oral mucositis (29% vs 89%,  $p < 0.001$ ) and its associated pain (18% vs 71%, visual analog score  $>7$ ,  $p < 0.001$ ), opioid analgesic use (7% vs 21%,  $p < 0.001$ ), and TPN (30% vs 39%,  $p < 0.039$ ), all during the last weeks of chemoradiotherapy. Patients in the treatment group also experienced reductions in 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).

Strengths of this study include its randomized and double-blind design and statistically significant findings across all outcomes measured. Limitations include the small sample size, the lack of follow-up to assess any long-term effects of LLLT treatment, and the low-middle income treatment context (i.e. India), which may limit generalizability to different patient populations. Investigators concluded that LLLT "can be considered a safe modality for treating chemoradiotherapy-induced oral mucositis."<sup>27</sup>

- In 2012, Gautam and colleagues also published results from a second RCT evaluating low-level laser therapy (LLLT) for prevention of chemoradiotherapy-induced oral mucositis in 220 patients with head and neck cancer.<sup>28</sup> This trial appears to include the 121 patients evaluated in the above study.<sup>27</sup> As with that study, patients in this larger RCT received LLLT before radiotherapy at 66 Gy delivered daily in 33 fractions, five days per week, concurrent with cisplatin. Investigators reported that LLLT patients ( $n=115$ ) experienced significant reductions compared to the placebo group ( $n=124$ ) in the incidence and duration of severe oral mucositis (8.19 days vs 12.86 days) and its associated pain (visual analog score approximately 4 vs 7), total parenteral nutrition (45.0% vs 65.5%), and opioid analgesic use (9% vs 26% for step III).

Strengths of this study include its randomized and double-blind design and statistically significant findings across all outcomes measured. Limitations include the lack of follow-up and the low-middle income treatment context (i.e. India), which may limit generalizability to different patient populations. Investigators reiterated their support for the use of LLLT in the treatment of oral mucositis among cancer patients.

### High-Power Laser Therapy

#### *Chronic Pain*

- In 2015 (updated 2018), ECRI conducted an evidence review evaluating high-intensity laser therapy (HILT) for the treatment of acute and chronic pain.<sup>29</sup> ECRI searched exclusively for systematic reviews and RCTs published through July 2018, assessing HILT's safety and effectiveness for acute or chronic pain ( $n > 10$ ). The review included 10 publications (1 systematic review and 9 RCTs), as well as the abstracts of 7 RCTs reporting on 1,288 patients. RCT sample sizes ranged from 30 to 91; mean follow-up duration was 3 months. The included systematic review,<sup>30</sup> comprising six RCTs ( $n = 395$ ), compared HILT alone or HILT plus other treatments with placebos, placebos plus other treatments, or other treatments only in patients with knee osteoarthritis and reported on pain (measured by visual analog scale). Investigators reported that HILT alone or in combination with other treatments reduced pain more than sham alone, sham plus other treatments, or other treatments without sham in patients with knee osteoarthritis. Six of 8 RCTs that compared HILT alone, or HILT plus other

treatments to sham laser treatment, or sham plus other treatments, reported that HILT reduced pain, whereas the remaining 2 RCT's reported no difference in pain relief between groups. Four of 8 RCTs that compared HILT alone, or HILT plus other treatments without sham laser treatment, reported HILT or HILT combined with other treatments reduced pain, while 3 RCTs reported no between-group differences.

Despite these positive results, ECRI noted a number of limitations among included studies, which undermined the validity. The RCT's included in the large systematic review were heterogeneous with varying treatment modalities, research protocols, treatment duration and reported follow-up periods. RCT's included for review suffered from small sample sizes, subjective patient-oriented outcomes, a lack of blinding, heterogeneous treatment combinations, heterogeneous comparators, and heterogeneous patient populations with pain attributable to varying clinical conditions. ECRI concluded that additional studies reporting on pain scores with longer-term follow-up (one year or more) were needed to establish HILT's efficacy and clinical utility.

#### *Additional Indications*

Several systematic reviews recently reported positive results for the use of HILT in the treatment of musculoskeletal disorders,<sup>31,32</sup> foot ulcers,<sup>33</sup> and knee osteoarthritis.<sup>34</sup> Nonetheless, these reviews call for additional, high-quality studies to determine the efficacy, safety and treatment parameters of HILT.

## CLINICAL PRACTICE GUIDELINES

### Low-Level Laser Therapy

#### *National Institute for Health and Care Excellence (NICE)*

In 2018, NICE issued an interventional procedures guidance addressing low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy.<sup>35</sup> Investigators stated that "evidence on efficacy is adequate in quality and quantity" and that LLLT for oral mucositis "can be used provided that standard arrangements are in place for clinical governance, consent and audit." This decision was made on the basis of evidence reported in 3 systematic reviews and meta-analysis, 7 randomized controlled trials and 1 non-randomized comparative study.

#### *American Academy of Orthopedic Surgeons (AAOS)*

The 2016 AAOS evidence-based clinical practice guideline on the treatment of carpal tunnel syndrome, states, "limited evidence supports that laser therapy might be effective compared to placebo. Strength of Recommendation: Limited Evidence."<sup>36</sup>

#### *American College of Physicians (ACP)*

The 2017 ACP evidence-based clinical practice guideline evaluating noninvasive treatments for acute, subacute, and chronic low back pain gave a recommendation based on low-quality evidence for low-level laser therapy.<sup>37,38</sup>

*Colorado Division of Worker's Compensation*

- The 2014 Colorado Division of Worker's Compensation evidence-based clinical practice guideline for low back pain did not recommend low-level laser therapy.<sup>39</sup>
- The 2015 Colorado Division of Worker's Compensation evidence-based clinical practice guideline for shoulder injury did not recommend low-level laser therapy.<sup>40</sup>

*American Physical Therapy Association*

- The 2013 American Physical Therapy Association evidence-based guideline for ankle stability and movement coordination impairments stated, "(t)here is moderate evidence both for and against the use of low-level laser therapy for the management of acute ankle sprains. (Grade of Recommendation D: conflicting evidence)."<sup>41</sup>
- The 2014 American Physical Therapy Association evidence-based clinical practice guideline for heel pain- plantar fasciitis gave a recommendation based on weak evidence for, "low-level laser therapy to reduce pain and activity limitations in individuals with heel pain/plantar fasciitis. (Grade of Recommendation C: weak evidence)"<sup>42</sup>

*Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO)*

In 2020, MASCC and ISOO updated guidelines on the management of mucositis secondary to cancer therapy. They recommend the following.<sup>43</sup>

1. A recommendation for the prevention of OM [oral mucositis] with intraoral PBM [photobiomodulation] therapy in patients who undergo HSCT [hematopoietic stem-cell transplantation] —the current systematic review reiterates the 2014 guidelines in this patient population and increases the range of PBM settings that may be used; (level of evidence= 1)
2. A recommendation for the prevention of OM with intraoral PBM therapy in patients with cancer who receive H&N [head and neck] RT [radiotherapy] (without CT [chemotherapy])—this is an upgrade of the 2014 guidelines from a suggestion to a recommendation; (level of evidence= 2)
3. A recommendation for the prevention of OM with intraoral PBM therapy in patients with cancer who receive H&N RT with CT —this new guideline is based on recent evidence. (level of evidence= 1)

In regards to treatment of OM, the guidelines state: "We identified several RCTs aimed at the treatment of OM in pediatric patients undergoing mixed RT/RT-CT, mixed HSCT/CT, or CT for several types of cancer. The results were promising; however, it is too early to base a guideline on these findings.

In 2014, the MASCC and ISOO issued a joint guideline recommending the use of LLLT for the prevention of oral mucositis in patients receiving hematopoietic stem cell transplantation (HSCT) conditioned with high-dose chemotherapy and for patients undergoing head and neck radiotherapy, without concomitant chemotherapy.<sup>44</sup> This recommendation was made largely on the basis of one, randomized placebo-

controlled trial,<sup>45</sup> which did not achieve statistical significance for its primary outcome. The guideline's recommendation for LLLT for patients undergoing radiotherapy with head and neck cancer was based on what investigators deemed "weaker evidence."<sup>44</sup>

#### High-Power Laser Therapy

No clinical practice guidelines were identified that evaluated high-power laser therapy for the treatment of clinical disorders.

## **CENTERS FOR MEDICARE & MEDICAID**

As of 6/4/2021, one relevant Centers for Medicare & Medicaid (CMS) guidance document was identified: National Coverage Determination (NCD) for Laser Procedures (140.5).<sup>46</sup> The NCD states:

"In the absence of a specific noncoverage instruction, and where a laser has been approved for marketing by the Food and Drug Administration, Medicare Administrative Contractor discretion may be used to determine whether a procedure performed with a laser is reasonable and necessary and, therefore, covered."<sup>46</sup>

Our Medicare administrative contractor, Noridian, does not address low-level or high-powered laser therapy, therefore commercial criteria will apply.

## **POLICY SUMMARY**

There is enough high-quality evidence to show that low-level laser therapy is an effective treatment for preventing oral mucositis in individuals undergoing cancer treatments that increase risk of oral mucositis. Systematic review of randomized trials have found that preventive use of low-level laser therapy reduced incidence and severity of oral mucositis in patients being treated with chemotherapy, radiotherapy, or hematopoietic stem cell transplant, or a combination of cancer therapies. Therefore, low-level laser therapy for the prevention of oral mucositis may be considered medically necessary.

Evidence is insufficient to support low-level laser therapy (i.e., cold laser therapy) or high-power laser therapy (class IV lasers) as effective treatments for any indication, including, but not limited to, carpal tunnel syndrome, hair loss, chronic low back pain, rotator cuff tendinopathy, pressure ulcers, and treating oral mucositis. Further studies of good methodological quality are required in order to establish the safety, effectiveness, and medical necessity of these treatment modalities. Clinical guidelines on low-level laser therapy have weak recommendations for its use based on low-quality evidence or recommend against the treatment. No evidence-based clinical practice guidelines were identified that evaluated high-power laser therapy. Therefore, low-level and high-power laser therapy are considered investigational as a treatment for any indication other than preventing oral mucositis.

## **INSTRUCTIONS FOR USE**

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed

annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days' notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

## **REGULATORY STATUS**

### **U.S. Food and Drug Administration (FDA)**

#### Low-Level Laser Therapy

The FDA has approved several low-level laser therapy devices including, but not limited to, the following:

- MicroLight ML830® (MicroLight Corporation of America)<sup>47</sup>
- GRT LITE™ PRO-8A (GRT Solutions, Inc.)<sup>48</sup>
- LightStream™ Low Level Laser (RJ Laser Canada Corp.)<sup>49</sup>
- TouchOne™ (OTC)<sup>50</sup>

Additional low-level laser therapy devices can be found by searching the FDA Devices Database for product code NHN.

#### High-Power Laser Therapy

The FDA has approved several high-power laser therapy devices including, but not limited to, the following:

- LCT-1000 (LiteCure, LLC)<sup>51</sup>
- ALT Laser (Avicenna Laser Technology, Inc.)<sup>52</sup>
- ESPT-3X (Lighthouse Technical Innovations, Inc.)<sup>53</sup>

Additional high-power laser therapy devices can be found by searching the FDA Devices Database for product code ILY.

### **Mental Health Parity Statement**

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

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