Clinical Policy Title: Laser treatment of port-wine stains and infantile hemangiomas

Clinical Policy Number: 16.03.04

Effective Date: January 1, 2015
Initial Review Date: September 17, 2014
Most Recent Review Date: September 21, 2017
Next Review Date: September 2018

Related policies:

None.

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of pulse dye laser treatment for port-wine stains or infantile hemangiomas to be clinically proven and, therefore, medically necessary when the following criteria are met:

I. Including, but not limited to port-wine stains or infantile hemangioma lesions that:
   - Are located where there is potential compromise or actual compromise of vital structures (e.g., nose, eyes, ears, lips, tongue or larynx) or
   - Are symptomatic (e.g., bleeding, painful, ulcerated, prior infection, or pedunculated and symptomatic) or
   - Involves the eyelids or periorbital tissue and result in impaired vision or strabismus or
   - Result in auditory impairment and secondary speech delay (lesions that are located on or around the ear) or
   - Result in a risk of bleeding caused by bleb formation or incidental trauma.
Infantile Hemangioma

Treatment modalities may include one or more of the following alone or in combination (not an all inclusive list):

a. Clinical observation (appropriate if not causing functional impairment).
b. Propranolol. (hospitalization may be necessary for infants)
c. Corticosteroids.
d. Laser therapy
e. Surgery
f. Radiotherapy
g. Sclerosing therapy
h. Cryosurgery/Cryotherapy

Port-Wine Stains

a. Pulsed dye laser therapy

Note: Depending on the extent of the port-wine stains, several laser treatments may be required, spaced at two- to three-month intervals.

Limitations:

All other uses of laser therapy to treat port-wine stains are not medically necessary, including the following:

- Laser treatment of port-wine stains that do not cause functional impairment.
- Treatment of port-wine stains with lasers, in combination with photodynamic therapy or topical angiogenesis inhibitors.
- Laser treatment for port-wine stains and infantile hemangioma is usually considered cosmetic in adults 21 years and older) without significant documentation of the functional affects.

Alternative covered services:

Consultation with dermatologist.

Background

Port-wine stains (nevus flammeus), are red or purple marks, often on the face. Port-wine stains represent the most common vascular malformation, and is commonly known as Firemark. They are caused by a localized area of abnormal blood vessels (capillaries). About three in 1,000 babies are born with port-wine stains. Most occur on the face but any area of the skin can be affected. Although the vast majority of port-wine stains are present at birth, they can occasionally develop later on. (CHOP, 2017; Cunliffe, 2012).

A modest percentage of port wine stains located over the eye and central forehead can be associated with glaucoma and/or complications in the brain resulting in seizures or developmental disabilities. This association of facial port-wine stains and glaucoma and/or seizures is called the Sturge-Weber
Syndrome. The location and the extent of the port-wine stains on one extremity can lead to enlargement of the extremity relative to an unaffected limb (Klippel-Trenaunay-Weber Syndrome).

In 2013, the cause of port-wine stains and Sturge-Weber Syndrome was discovered. A somatic activating mutation in the guanine nucleotide-binding protein was identified in 12 of 13 cases of port-wine stains and 23 of 26 cases of Sturge-Weber Syndrome, confirming a long-standing hypothesis (Shirley, 2013).

There are several types of laser systems available for port-wine stains. The Flashlamp-Pulsed Dye Laser (FPD-PL) is the gold standard for port-wine stains treatment. It emits a yellow light wave length of 595 to 600 nanometers, which allow deeper penetration than the original 577 nm models introduced in the 1980s (Brightman, 2015). Pulsed dye lasers target oxyhemoglobin and deoxyhemoglobin. The pulsed dye laser penetrates up to 2 millimeters of skin with a duration of just milliseconds. The procedure is delivered in outpatient settings, over multiple sessions, with or without anesthesia (CHOP, 2017; Cunliffe, 2012).

Infantile hemangiomas are the most common (benign) childhood tumors. They develop within 4 – 6 weeks of birth, and are present in 1-3 percent of newborns, and in 10 – 20 percent of infants under age one (Darrow, 2015). In newborns under 1000 grams, the rate can be as high as 22 – 30 percent (Zang, 2013). Up to 70 percent of cases lead to residual skin changes. Complications include ulceration, bleeding, feeding problems, and visual impairment (Randel, 2016).

Infantile hemangiomas can also be associated with a constellation of congenital anomalies:

- Posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye abnormalities, sternal cleft and supraumbilical raphe (PHACES syndrome).
- Perineal hemangioma, external genitalia malformations, lipomyelomeningocele, vesicorenal abnormalities, imperforate anus and skin tag (PELVIS syndrome).
- Lower-body hemangioma and other cutaneous defects, urogenital anomalies, ulceration, myelopathy, bony deformities, anorectal malformations, arterial anomalies and renal anomalies (LUMBAR syndrome).

A distant subset of infantile hemangiomas consists of multiple small lesions varying in size from a few millimeters to one to two centimeters. This form of infantile hemangioma (so-called multiple neonatal hemangiomatosis) has a higher risk of visceral involvement, particularly in the liver and gastrointestinal tract; however, the prognosis for the skin lesions is usually good, as they often involute by two years of age.

After laser therapy for infantile hemangioma, the area will often turn off-white within 7 – 14 days. An evaluation should be made every 2 – 4 weeks after treatment until the condition is resolved, or another treatment is needed (Zhang, 2013).
The U.S. Food and Drug Administration (FDA) has approved lasers for marketing, through the 510(k) process, for a variety of dermatologic indications, including treatment of port-wine stains. Approved lasers for this indication include the Candela Vbeam® pulsed dye laser system (Candela Corp.; Wayland, MA), the Cynosure Photogenica® pulsed dye laser (Cynosure Inc.; Westford, MA) and the Cynosure Nd: YAG laser system. In addition, the Cynergy™ MultiPlex Laser™ (Cynosure), a combined Nd: YAG and pulsed dye laser, was approved by the FDA in 2005 for treatment of benign vascular and vascular dependent lesions, including port-wine stains. In 2003, the Lumenis® family of intense pulsed light systems was approved by the FDA; indications for use include dermatological applications. Subsequently, the NannoLight™ intense pulsed light system (Sybaritic) was approved by the FDA in 2008 and the MDFLASH4 and STFLASH4 systems (Dermeo®) were approved in 2010 for indications specifically including treatment of port-wine stains.

**Searches**

Select Health of South Carolina searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 4, 2017. Search terms were: “Port wine stain,” “infantile hemangioma” and “laser treatment” (MeSH).

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

No specific professional guidelines exist for treating port-wine stains. A 2015 review of the literature finds that lasers, in particular, pulsed dye lasers are effective modes of treatment for port-wine stains, asserting that 80 to 90 percent improvements are common in early and optimal treatments (Brightman, 2015).
An American Academy of Pediatrics guideline notes that after 2008, systemic corticosteroids, in particular propranolol, have been used to treat infantile hemangioma. The guideline recommends the drug, with cardiovascular monitoring every hour for two hours, with repeat monitoring for any dose increase over 5 mg/kg. If propranolol can’t be used or is ineffective, corticosteroids (usually daily oral prednisone or prednisolone) can be an alternative therapy. Laser therapy may be useful in treating early lesions (Randel, 2016).

A summary of recommended therapies for infantile hemangioma includes lasers, along with chemotherapy, Interferon alpha 2a, systemic or intralesional steroids, radio- or cryo-therapy, therapeutic embolization, and surgery (Fette, 2013). Another guideline states that laser therapy for infantile hemangioma be repeated every 2 – 4 weeks, and that it is not suitable for deep-seated hemangiomas (Zhang, 2013).

PORT-WINE STAINS RESULTS:

A Hayes review of 22 studies, only eight of which were randomized, determined that pulsed dye laser is a standard treatment for port-wine stains, but as up to 30 percent of lesions are resistant to current treatment modalities, new therapies are needed. Moreover, Hayes authors analyzed five trials (just two randomized) for pulsed dye laser efficacy for infantile hemangioma, and concluded this treatment remains “controversial” as treatment is recommended only for superficial involuting or ulcerating hemangiomas, but not for deep or mixed hemangiomas (Hayes, 2016).

One large non-randomized study on pulsed dye laser for port-wine stains included 848 cases, using a 595 nm laser. The response rate was 69.9 percent, and the cure rate among respondents was 6.3 percent. The response for infants under age one was 93.3 percent, significantly greater than those older than 50. The temporal region had the highest clearance rate of 75.5 percent, while the rate for extremities was just 44.5 percent. Patients with lesion size of 0-20 cm had a higher rate of clearance than those larger than 80 cm, 73.8 versus 53.2 percent. Finally, early intervention was associated with higher clearance rates (Shi, 2014).

An RCT compared (single-session) pulsed dye laser treatment with vascular-targeted photodynamic therapy in 15 port-wine stains patients age 11 to 36, using adjacent flat areas of lesions. For both red and purple lesions, photodynamic therapy showed equal or higher blanching improvements than did pulsed dye laser (Gao, 2013). Another RCT compared pulsed dye laser with intense pulsed light for port-wine stains in a randomized side-by-side trial in 20 patients with port-wine stains. Both treatments resulted in clinical improvements, but were significantly better for pulsed dye laser (65 versus 30 percent, p = .0004). Improvement in skin lightening was also superior for pulsed dye laser (33 versus 12 percent, p=.002). All but two of the 20 patients preferred to receive continued treatment with pulsed dye laser (Faurschou, 2009). A study of 158 port-wine stains spots in pulsed dye laser patients found that intense pulsed light treatments were significantly better in clearing lesions than did pulsed dye laser (Babilas, 2010).
Combining pulsed dye laser with other treatments has been done in several studies. The most recent RCT of pulsed dye laser treatment was a trial of 23 patients that compared four groups with port-wine stains; placebo, pulsed dye laser plus placebo, rapamycin alone, and pulsed dye laser plus rapamycin. Combining pulsed dye laser and rapamycin yielded the lowest digital photographic image score and lowest percent of vessels, and a significant improvement versus other interventions (Marques, 2015). Adding imiquimod 5 percent cream to pulsed dye laser in 24 patients with port-wine stains resulted in greater change in erythema in combination sites versus pulsed dye laser plus placebo sites (p<.03), and greater change in color in combination sites (p<.04) (Tremaine, 2012).

In 26 patients with port-wine stains treated with a minimum of three double-pass pulsed dye laser treatments alone, or in combination, with single pass conventional pulsed dye laser, 12 showed a moderate or significant improvement, and another 12 a mild improvement, in fading, compared to pre-treatment photographs with the double-pass technique. Many patients developed mild side-effects, including blisters (n = 5), dry scabs (n = 11) and transient hyperpigmentation (n = 4) (Rajaratnam, 2011).

Pain is a common side effect after laser therapy for dermatological procedures for conditions such as port-wine stains. A review of 32 randomized and non-randomized controlled studies showed that non-invasive techniques including pulsed dye laser resulted in less pain than placebo, and topical anesthesia had better outcomes than skin cooling (Greveling, 2017).

**INFANTILE HEMANGIOMA RESULTS:**

A Cochrane review of five studies (n=103) of infantile hemangioma treatment with various laser therapies showed subjects marginally preferred yttrium-aluminum garnet lasers to pulsed dye therapy. However, 1 – 3 pulsed dye laser treatments over 4 – 6 months produced a reduction of at least 25 percent in redness, described by the authors as “clinically relevant clearance” (Faurschou, 2011). Another Cochrane review of four studies (n=271) included a single RCT that observed pulsed dye laser was (significantly) more likely to result in complete resolution of pulsed dye laser than a “wait and see” approach; pulsed dye laser patients experienced less redness, but had higher increases in atrophy and skin hypopigmentation. Authors concluded that more RCTs were needed to confirm results such as this (Leonardi-Bee, 2011).

A meta-analysis of 13 studies (n=1580) showed an 89.1 percent resolution rate and a 6.28 percent adverse effect rate of pulsed dye laser on infantile hemangioma (Shen, 2015).

An Agency for Healthcare Quality and Research review of 148 studies of infantile hemangioma outcomes indicated that longer-pulse pulsed dye laser was generally more effective than observation (Chinnadurai, 2016a). This finding was consistent in a review of 29 studies, which also concluded that pulsed dye laser worked better than other laser therapies (Chinnadurai, 2016b).
A 2016 study of 647 patients with a variety of diseases, including infantile hemangioma, found use of the relatively new potassium-titanyl phosphate laser resulted in only 5.8 percent of patients with adverse effects, and only one patient with bruising, rates lower than for pulsed dye laser (Becher, 2014).

Policy updates:

A total of 5 guidelines/other and 18 peer-reviewed references were added to this policy in 2017, and 1 guidelines/other and 24 peer-reviewed references were removed.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hayes (2016)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Pulsed dye therapy</td>
<td>• Hayes review of pulsed dye therapy for PWS (22 studies, 8 randomized) and IH (5 studies, 2 randomized)</td>
</tr>
<tr>
<td>(PDT) for port wine</td>
<td>• For PWS, PDL therapy is a standard treatment, but up to 30% of lesions are resistant to treatment, and new therapies are needed</td>
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<tr>
<td>stains (PWS) and</td>
<td>• For IH, treatment recommendations vary by the type and stage of hemangioma; PDL is recommended for superficial involuting or ulcerating hemangiomas, but not for deep or mixed hemangiomas</td>
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<tr>
<td>infantile hemangioma</td>
<td></td>
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<tr>
<td>(IH)</td>
<td></td>
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<tr>
<td>Shen (2015)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>PDL for IH</td>
<td>• Systematic review and meta-analysis for IH, included 13 articles (n=1529)</td>
</tr>
<tr>
<td></td>
<td>• Overall resolution rate was 8.1%</td>
</tr>
<tr>
<td></td>
<td>• Incidence of adverse effects was 6.28%</td>
</tr>
<tr>
<td>Shi (2014)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Outcomes of PHS</td>
<td>• Descriptive study of 848 PWS patients in China</td>
</tr>
<tr>
<td>treatment with PDL</td>
<td>• Response rate (RR) of patients = 69.9%, of which 6.3% were cured</td>
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<td></td>
<td>• RR higher for age &lt;1 (93.9%) vs. age &gt; 50</td>
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<td></td>
<td>• RR highest for temporal region (75.3%) vs. extremities (44.5%)</td>
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<td></td>
<td>• RR highest for small lesions &lt;20 cm (73.8%) vs. &gt;80 cm (53.2%)</td>
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<tr>
<td>Faurschou (2011)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Lasers for treating</td>
<td>• Cochrane review of 5 randomized controlled trials (n=103)</td>
</tr>
<tr>
<td>PWS</td>
<td>• Participants preferred DPL to intense pulsed light</td>
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<td></td>
<td>• Participants preferred yttrium-aluminum-garnet to PDL</td>
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<tr>
<td></td>
<td>• Participants preferred PDL with cooling to PDL alone</td>
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<tr>
<td></td>
<td>• PDL resulted in more than 25% reduction in redness, after 1-3 treatments for up to 4-6 months postoperatively</td>
</tr>
</tbody>
</table>

References

Professional society guidelines/other:


**Peer-reviewed references:**


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


**Local Coverage Determinations (LCDs):**


**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<td>17106</td>
<td>Destruction of cutaneous vascular proliferative lesions (e.g., laser technique); less than 10 sq cm.</td>
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<td>17107</td>
<td>Destruction of cutaneous vascular proliferative lesion (e.g., laser technique); 10.0 to 50.0 sq cm.</td>
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<td>17108</td>
<td>Destruction of cutaneous vascular proliferative lesion (e.g., laser technique); over 50.0 sq cm.</td>
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<thead>
<tr>
<th>ICD-10 Code</th>
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<tr>
<td>Q82.5</td>
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<tr>
<td>D18.00</td>
<td>Hemangioma unspecified site</td>
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<td>D18.01</td>
<td>Hemangioma of skin and subcutaneous tissue</td>
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<tr>
<td>D18.02</td>
<td>Hemangioma of intracranial structures</td>
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<tr>
<td>D18.03</td>
<td>Hemangioma of intra-abdominal structures</td>
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<tr>
<td>D18.09</td>
<td>Hemangioma of other sites</td>
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<tr>
<th>HCPCS Level II Code</th>
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