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, 2016
Next Review Date: September 2017

Related policies:

None.

ABOUT THIS POLICY: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania’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 AmeriHealth Caritas Pennsylvania 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. AmeriHealth Caritas Pennsylvania’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. AmeriHealth Caritas Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Pennsylvania considers the treatment for port-wine stains (PWS) and infantile hemangiomas (IH) to be clinically proven and, therefore, medically necessary when the following criteria are met:

Including, but not limited to PWS or IH lesions:

- That are located where there is potential compromise or actual compromise of vital structures (e.g., nose, eyes, ears, lips, tongue or larynx).
- That are symptomatic (e.g., bleeding, painful, ulcerated, prior infection, or pedunculated and symptomatic).
- That involves the eyelids or periorbital tissue and result in impaired vision or strabismus, facial long term permanent- disfigurement, airway obstruction and liver
- That result in auditory impairment and secondary speech delay (lesions that are located on or around the ear).
- That result in a risk of bleeding caused by bleb formation or incidental trauma.
- IH lesions that involve areas of moisture or friction (e.g. lips, perineum).

**Infantile Hemangiomas**

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 Stain**

- a. Pulsed dye laser therapy

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

**Limitations:**

All other uses of laser therapy to treat PWS are not medically necessary, including the following:

- Laser treatment of PWS that do not cause functional impairment is not medically necessary.
- Treatment of PWS with lasers, in combination with photodynamic therapy or topical angiogenesis inhibitors, is considered investigational.
- Laser treatment for PWS and IH is usually considered cosmetic in adults (21 years and older), and not medically necessary without significant documentation of the functional affects.

**Alternative covered services:**

Consultation with dermatologist.

**Background**

PWS (nevus flammeus), are red or purple marks, often on the face. They are caused by a localized area of abnormal blood vessels (capillaries). About three in 1,000 babies are born with a PWS. Most occur on the face but any area of the skin can be affected. Although the vast majority of PWS are present at birth, they can occasionally develop later on. Possible causes include long-term exposure to ultraviolet light,
other types of skin damage and changes in hormone levels. Infections, rare brain tumors and conditions affecting the blood vessels inside the body may also be involved.

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 PWS and glaucoma and/or seizures is called the Sturge-Weber Syndrome. Depending on the location and the extent of the PWS on one extremity can lead to enlargement of the extremity relative to an unaffected limb (Klippel-Trenaunay-Weber Syndrome)

There are several types of laser systems available. The Flashlamp-Pulsed Dye Laser (Candela) is the gold standard for PWS treatment and offers several distinctive advantages over other systems. It was specially designed to treat the PWS and for other skin lesions with prominent red blood vessels. This Laser is often used without anesthesia, has a very low risk of scarring, and is safe and effective for use on infants and children as well as adults. The current device, the Vbeam, comes equipped with a synchronized dynamic cooling device to protect the skin’s surface so that higher energies can be delivered to the skin safely and to minimize the pain with treatment. In addition, this Laser has the capacity to deliver longer pulses which allow the energy to more effectively heat and destroy larger vessel targets and avoid bruising. The Vbeam has a slightly longer wavelength as well as larger spot sizes, which allow deeper Laser penetration and has higher energy fluences to more effectively destroy the vessel targets (Katugampola GA, 1997).

IH are the most common childhood tumors. IH are vascular tumors that, while benign, have potential for local tissue destruction, infection, bleeding and pain. Due to historical inconsistencies in naming conventions, it is difficult to understand the true prevalence of IH; it has been suggested that they affect about 4 percent to 5 percent of children, with higher prevalence in females and Caucasians. The most common locations are the head, neck and trunk, but they can occur almost anywhere throughout the body, including deep compartments of the extremities, the spine and visceral organs. IH 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).

IH tend to go through growth, plateau and involution phases, although the complete natural history of IH by various characteristics has not been described. IH becomes apparent in most patients in the first few weeks of life and reach 80 percent of total size by around the age of 3 months. With a course of expectant observation, many patients may experience a complete involution without significant sequelae; however, IH frequently occurs in cosmetically and functionally sensitive areas. Even with
complete involution, some patients have permanent cosmetic disfigurement and functional compromise. Early assessment of the extent of the IH and early, appropriate treatment of IH may potentially mitigate these complications. Furthermore, some lesions are particularly aggressive or morbid and can cause severe pain, ulceration and bleeding even in early stages. With this rapid growth, there is little time for prospective observation to determine which hemangiomas will lead to complications and require specialist attention and treatment before complications begin to manifest. Some types of IH, specifically segmental hemangiomas such as those associated with syndromes like PHACES, are recognized as high risk, but no consensus exists on which nonsegmental lesions warrant referral for appropriate treatment to mitigate future complications (e.g., bleeding or ulceration) of the hemangioma or long-term sequelae (e.g., scarring, anatomical disfigurement, and functional complications).

Several clinical subtypes of hemangiomas are recognized:

- **Superficial (so-called “strawberry”) hemangiomas** are most common, constituting 50 percent to 60 percent of tumors. Those with both a superficial and deep component (previously referred to as “capillary and cavernous or missed”) constitute approximately 25 percent to 35 percent of lesions and contain both a red dermal tumor and an underlying blue or skin-colored subcutaneous mass.
- **Deep hemangiomas** (formerly called “cavernous hemangiomas”) constitute approximately 15 percent of hemangiomas and are usually bluish soft-tissue swellings without an overlying superficial component.
- Despite difference in clinical appearance, all are true hemangiomas with the same fundamental characteristic. Multiple lesions are present in 15 percent to 30 percent of infants.

Many therapies have been used to treat PWS. Most therapies, such as surgery, radiation, X-ray, dry ice or tattooing have been abandoned because these treatments often leave malformations as undesirable as the PWS itself.

A distant subset of IH consists of multiple small lesions varying in size from a few millimeters to one to two centimeters. This form of IH (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.

Laser therapies available are the flashlamp-pulsed dye laser (Candela). This is the gold standard for PWS treatment and offers several advantages over other systems. It was specially designed to treat PWS and other skin lesions with prominent red blood vessels. This laser can often be used without anesthesia, has a very low risk of scarring, and is safe and effective for use on infants and children and adults. The current device, the Vbeam, comes equipped with a synchronized dynamic cooling device to protect the skin’s surface so that higher energies can be delivered to the skin safely and minimize pain. In addition, this laser has the capacity to deliver longer pulses, which allow the energy to more effectively heat and
destroy larger vessel targets and avoid bruising. The Vbeam has a slightly longer wavelength, as well as larger spot sizes, which allows deeper laser penetration and has higher energy fluences to more effectively destroy the vessel targets. Currently, the most common in clinical practice is the pulsed dye laser (PDL) which uses yellow light wavelengths (585 – 600nm) that selectively target both oxyhemoglobin and deoxyhemoglobin.

There are a number of promising experimental therapies for PWS currently being investigated. Several of these modalities are photodynamic therapy (PDT), angiogenesis inhibitors, hemodynamic alterations in PWS vasculature and site-specific pharmaco-laser therapy. PDT involves the activation of a photosensitizer by visible light. The absorption of light triggers a photochemical-biological reaction that, in the presence of oxygen, leads to reactive oxygen species generation, which causes direct endothelial cell damage, thrombosis and shutdown of vasculature. Overall, PDT-PDL combination therapy appears promising, although additional controlled clinical trials are needed to evaluate the efficacy, safety and advantages of the combined therapy.

The U.S. Food and Drug Administration (FDA) have cleared lasers for marketing, through the 510(k) process, for a variety of dermatologic indications, including treatment of PWS. 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 PWS. 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 PWS.

Pharmacological treatments like corticosteroids have been the first-line treatment for IH for more than 40 years (Zarem and Edgerton, 1967; Cohen and Wang, 1972). Recently, beta blockers, most specifically propranolol, have been shown to be an effective pharmacological treatment of proliferating IH. Other less common medications are interferon-2α and vincristine (Maguiness and Frieden, 2010). Propranolol, as a pharmacological treatment of IH, was first reported in 2008, in two children who showed rapid regression of disease when treated with propranolol for cardiopulmonary indications (Leaute-Labreze et al., 2008). Since then, propranolol treatment for IH has become popular worldwide and positive results with its use are reported by many groups (Cheng et al., 2010; Mazereeuw-Hautier et al., 2010; Rosbe et al., 2010). Propranolol is a noncardioselective β-adrenergic receptor blocker used traditionally for other indications such as hypertension, angina pectoris, myocardial infarction, migraines, anxiety disorders and tremor. The mechanism of action of propranolol on IH remains elusive. To date there are no studies on the effects of propranolol using IH animal models or cultured IH-derived cells. Therefore, in summary, the general mechanisms of action of propranolol suggest possible mechanisms based on data derived from studies performed using angiogenesis assays and endothelial cells. Propranolol was approved by the FDA for use in hemangiomas in March 2014. Prior to this, corticosteroids were the drug of choice, and discord still exists about which represents the best choice for initial medical management.
Additionally, there is no clear consensus when alternative or adjunctive medications, such as chemotherapeutic drugs, are appropriate after first-line treatment is unsuccessful.

Cosmetic camouflage creams can be used to help to conceal the PWS. It is more effective than over-the-counter foundation or makeup because it is lightweight and available in a wide range of colors.

**Searches**

AmeriHealth Caritas Pennsylvania 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 22, 2016. Search terms were: “Pediatric congenital conditions, port wine stain, 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:**

According to the study, “An overview of clinical and experimental treatment modalities for port wine stains,” by Jennifer K. Chen, et al. (2012; American Academy of Dermatology), the pulsed dye laser currently remains the treatment of choice for PWS lesions. Despite innovations in various laser techniques and applications, the number of PWS refractory to current treatment modalities remains substantial. New experimental modalities are currently under investigation, including the use of photodynamic therapy, immune modulators, angiogenesis inhibitors, hemodynamic alterations in PWS vasculature and site-specific pharmacolaser therapy. Alternative therapies will be required to increase the efficacy of PWS treatment.

**Policy updates**

2015: Added recruiting clinical trials and related closed trials.
2016: Added background information and reference. Updated links, clinical trials and LCD.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tr>
<td>Li YC, et al. (2010)</td>
<td><strong>Key points:</strong></td>
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| Successful treatment of infantile hemangiomas of the orbit with propranolol: | - Background: Propranolol is a novel therapeutic agent in the treatment of cutaneous IH. Assessed the effect of propranolol therapy in IH of the orbit.  
  - Methods: A case series of four patients with orbital IH were referred for management. Two patients had inadequate responses to prior corticosteroid therapy. One patient was started on use of propranolol at age 2 1/2 when the lesion was not in the proliferative phase. This represented the first case report of propranolol treatment for IH outside infancy. The other three children were in their infancy when propranolol was commenced. The patients were treated with oral propranolol.  
  - Results: All patients had significant improvement in their physical appearance, ocular examination findings and size of their lesions on radiological evaluation. No side effects of propranolol treatment were observed.  
  - Conclusions: Propranolol is a promising treatment against IH in the orbit, not only in infants but also in older children with a stable lesion. |
| Ricci, et al, (1998)          | **Key points:**                   |
| Treatment of cutaneous hemangiomas in preterm neonatal twins with the flashlamp-pumped pulsed dye laser. | - Background and objective: Report of two cases of IH in twins born at a gestational age of 30 weeks who were treated with a flashlamp-pumped pulsed dye laser (FPDL) at 40 days postpartum. To the researchers' knowledge, these were the youngest patients to be treated with FPDL.  
  - Study design/patients and methods: Twin Caucasian females were born 10 weeks preterm. Twin A soon developed a 1 cm blanching erythematous patch with telangiectasia on a slightly bulbous nasal tip. Twin B developed a 6 mm erythematous papule on her forehead, a 12 x 10 cm erythematous plaque on her left shoulder, and two plaques measuring 2.5 x 2.0 cm and 1.5 x 1.0 cm on her right hip. The twins received seven monthly laser treatments.  
  - Results: Several of the hemangiomas showed remarkable regression, including the lesions that became ulcerated and healed on Twin B's left shoulder and right hip. No general or topical anesthesia was used and the twins tolerated the procedure well. No significant adverse effects were encountered. The maximum single treatment dose was 7 mm spot size, 5.0 J/cm² and 186 pulses for twin B and 6.25 J/cm² and 16 pulses for Twin A.  
  - Conclusion: To the researchers’ knowledge, these patients are the youngest reported to be treated with FPDL at age 30 days preterm. Some of their hemangiomas responded, and no significant adverse effects were encountered. More prospective trials are needed to determine whether early treatment with FPDL accelerates regression of hemangiomas or results in a better cosmetic outcome than expectant treatment. |
Huikeshoven M et al. (2007)  
**Key points:**

- Although pulsed-dye-laser therapy is currently the gold standard for the treatment of port-wine stains, few objective data are available on its long-term efficacy. Using objective color measurements, we performed a 10-year follow-up of a previously conducted prospective clinical study of the treatment of port-wine stains with a pulsed-dye laser.
- Of the 89 patients from whom color measurements were obtained in the previous study, 51 were included in this study. The median length of follow-up was 9.5 years. On average, the stain when measured at follow-up was significantly darker than it was when measured after the last of the initial five laser treatments (P=0.001), but it was still significantly lighter than it was when measured before treatment (P<0.001).
- Fifty-nine percent of patients were satisfied with the overall treatment result. Six percent of patients reported that the stain had become lighter since their last treatment, 59% that it was unchanged, and 35% that it had become darker.
- Using objective color measurements, we observed significant redarkening of port-wine stains at long-term follow-up after pulsed-dye-laser therapy. Patients should be informed about the possibility of redarkening before beginning treatment.

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**Glossary**

**Capillary malformation (CM)** — An inborn vascular malformation. Other terms are "port-wine stain" or "nevus flammeus." The capillaries, the smallest vessels, extend abnormally in the skin or tissue.

**Infantile hemangiomas (IH)** — A hemangioma is a birthmark that most commonly appears as a rubbery, bright red nodule of extra blood vessels in the skin. These may not be visibly present at birth but develop within the first few months of life.

**Klippel–Trénaunay syndrome (KT)** — A rare condition, characterized by the triad of cutaneous capillary malformations, usually PWS; soft tissue and bone hypertrophy (occasionally hypotrophy), usually of one lower limb; and varicose veins or venous malformations.

**Medically Necessary** — A service or benefit is Medically Necessary if it is compensable under the MA Program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.
**PHACE syndrome** — Posterior fossa malformations, hemangioma, arterial anomalies, cardiac defects, eye abnormalities, sternal cleft and supraumbilical raphe syndrome is a cutaneous condition with multiple congenital abnormalities.

**Port-wine stains (PWS)** — Red or purple marks, often on the face. Caused by a localized area of abnormal blood vessels (capillaries).

**Skin camouflage** — A common way of covering PWS. Special colored creams can be applied to PWS to improve the skin's appearance. The aim is to find a color to match the normal skin. Some cover creams can be prescribed on the NHS. Camouflage creams can disguise PWS very well, which may greatly increase self-confidence.

**Sturge–Weber syndrome (SWS)** — A neurocutaneous disorder classically presenting with:
- A facial PWS affecting the facial skin (in the distribution of some or all divisions of the trigeminal nerve).
- Vascular eye abnormalities.
- An ipsilateral occipital leptomeningeal angioma.
- The leptomeningeal malformations lead to venous hypertension and subsequent hypoperfusion of the underlying cortex.

**Wyburn-Mason syndrome** — This is also called unilateral retinocephalic syndrome and Bonnet-Dechaume-Blanc syndrome. There are facial PWS with unilateral AV malformation of the retina and intracranial optic nerves. Lesions may occur anywhere on the face. There may be facial hypertrophy or occasional involvement of the optic chiasm, the hypothalamus, the midbrain and the basal ganglia, with associated general learning disability or neurological features.

**References**

**Professional society guidelines/other:**


Peer-reviewed references:


**Clinical trials:**

Searched clinicaltrials.gov on August 22, 2016, using terms port wine stain and treatment | Open Studies. Three studies found, two relevant.

Massachusetts General Hospital Boston, Massachusetts, Preventing Growth of Hemangioma Tumors in Newborn: A Prospective Randomized Clinical Study. Updated: April 2016 ClinicalTrials.gov: [https://clinicaltrials.gov/ct2/show/NCT01873131?](https://clinicaltrials.gov/ct2/show/NCT01873131?).


**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.

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<td>Destruction of cutaneous vascular proliferative lesion (e.g., laser technique); over 50.0 sq cm.</td>
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