Cigna Medical Coverage Policy

Subject **Treatment of Cutaneous and/or Deep Tissue Hemangioma, Port Wine Stain and Other Vascular Lesions**

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Hyperlink to Related Coverage Policies

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Coverage Policy

Coverage for the treatment of a cutaneous hemangioma, port wine stain, or other vascular lesion is dependent upon benefit plan language, may be subject to the provisions of a cosmetic and/or reconstructive benefit and may be governed by state mandates.

Under many benefit plans, the treatment of a cutaneous hemangioma, port wine stain, or other vascular lesion is not covered when performed solely for the purpose of improving or altering appearance or self-esteem, or to treat psychological symptomatology or psychosocial complaints related to one's appearance.

Please refer to the applicable benefit plan document to determine the terms, limitations and conditions of coverage.

If coverage is available for treatment of a cutaneous and/or deep tissue hemangioma, port wine stain, or other vascular lesion, the following conditions of coverage apply.

Cigna covers laser destruction (CPT codes 17106, 17107, 17108) of cutaneous vascular lesions as medically necessary for EITHER of the following conditions:

- port wine stain and EITHER of the following indications:
  - the lesion results in bleeding or painful nodules
  - the lesion results in obstructed vision

- cutaneous and/or deep hemangioma or other vascular malformation (e.g., venous, arteriovenous, lymphatic) and EITHER of the following indications:
    - the lesion is affecting a vital structure (e.g., nose, eyes, ears, lips, or larynx)
    - the lesion results in **ANY** of the following:
        - bleeding
        - pain
        - ulceration
        - repeated infection
        - eating difficulty
        - swallowing difficulty

Cigna covers vascular embolization/occlusion (CPT codes 61626, 37241, 37242) of cutaneous and/or deep tissue hemangioma or other vascular malformation (e.g., venous, arteriovenous, lymphatic) as medically necessary for EITHER of the following indications:

- the lesion is affecting a vital structure (e.g., nose, eyes, ears, lips, or larynx)
- the lesion results in **ANY** of the following:
    - bleeding
    - pain
    - ulceration
    - repeated infection
    - eating difficulty
    - swallowing difficulty

INPATIENT HOSPITALIZATION

Cigna covers inpatient hospitalization of an infant for administration of oral propranolol for the treatment of cutaneous and/or deep tissue hemangioma as medically necessary when the lesion is ulcerated or affecting a vital structure (e.g., nose, eyes, ears, lips, larynx) and the infant is either of the following:

- age 8 weeks or less
- age 9 weeks to 12 months with ANY of the following:
    - lack of social support for home monitoring
    - presence of comorbid cardiovascular or respiratory conditions
    - presence of a comorbid condition affecting glucose levels

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General Background

Vascular lesions may be classified into two main categories: vascular tumors and vascular malformations. Vascular tumors are characterized by vascular endothelial cell hyperplasia and spontaneous involution. The most common vascular tumors are hemangiomas.

Vascular malformations are abnormalities in blood vessel formation; the lesions do not regress and slowly enlarge. The name of the malformation reflects the blood vessel forming the lesion: capillary, venous, arterial or lymphatic. A common capillary malformation, the port wine stain, is characterized by flattened endothelial cells with normal turnover. Venous malformations give a bluish color to the area under the involved skin or mucosa. Arterial malformations are rare, are often referred to as arteriovenous malformations and are direct connections of arteries to veins. Lymphatic malformations can involve either large (cystic hygroma) or small vessels (lyphangioma circumscriptum). Vascular malformations can also consist of combinations, such as with Klippel-Trenaunay Syndrome or Sturge-Weber Syndrome.

Vascular lesions may result in permanent disfigurement with the main goal of treatment aimed at improving cosmesis. However, some vascular lesions interfere with functioning of vital structures or result in symptoms, such as pain, ulceration and bleeding. Treatments are dependent on the type and severity of the lesion but

generally include injectable medications, laser therapy, sclerotherapy, embolization, surgical debulking, and compression garments; radiotherapy may be used in some cases.

Cutaneous/Deep Tissue Hemangiomas
Cutaneous hemangiomas occur in approximately 1 out of 10 children; these lesions are characterized by rapid proliferation in early infancy and slow involution that may occur over several years. The mechanisms that control involution are not well understood. Some hemangiomas are present at birth as precursor lesions; rarely are they fully formed tumors at birth (AAD, 2010). More commonly, lesions become evident after birth, usually within two to four weeks. Hemangiomas frequently occur on the face and neck area but may also be located on areas such as the trunk and/or internal organ structures. Most hemangiomas do not require medical intervention, although a small number cause functional complications or disfigurement. Permanent disfigurement is more likely if lesions are present on the face; the nose, lip, and forehead are most vulnerable (Conlon and Drolet, 2004).

Several types of congenital hemangiomas have been described in the literature and include those that are rapidly involuting, and noninvoluting. Kasabach-Merritt syndrome is a complication of rapidly enlarging vascular lesions (hemangioma) and is characterized by hemolytic anemia, thrombocytopenia and coagulopathy. While these lesions are not hemangiomas of infancy, they result from a more aggressive proliferative vascular tumor that results in decreased platelets and other bleeding problems. Although the syndrome is rare it requires aggressive treatment and is often associated with a high mortality rate.

For a majority of hemangiomas no intervention is needed and lesions regress spontaneously. Some lesions result in untoward cosmetic changes that have no clinical significance. However, complications resulting from hemangiomas have been reported and are often related to the site of occurrence, with approximately 10% of cases requiring treatment (Menezes, 2011). The most frequent complication associated with hemangiomas is ulceration which is often present during the proliferative phase. Periorbital hemangiomas may cause ambylopia, impaired vision and astigmatism and should be considered when a hemangioma involves the eyelids or periorbital tissue. Approximately 43-60% of individuals with periocular lesions can develop ambylopia (Al Dhaybi, et al., 2011, Leaute-Labreze, et al., 2011). Lesions located on the ear may result in auditory impairment and secondary speech delay. Subglottic hemangiomas may cause hoarseness and stridor leading to respiratory impairment and are associated with at least 50% mortality if untreated (Peridis, et al., 2011). Many patients with subglottic hemangiomas also have cutaneous hemangiomas involving the lips, chin, and mandible (beard area). Hemangiomas may also be located on the cervicofacial area and lumbosacral spine. Pedunculated hemangiomas may be at risk for bleeding and irritation and have been associated with permanent cosmetic skin changes after involution such as fibrofatty tissue and excessive scarring.

The main goals of treatment include preventing permanent disfigurement and minimizing psychosocial distress, preventing functional complications, and treating ulceration. Several modalities have been proven effective to treat hemangiomas and include the administration of steroid medications as the mainstay of treatment (e.g., topical, intralesional and systemic), pulsed dye laser therapy, and interferon. Corticosteroids have been associated with significant adverse events such as Cushing's syndrome, hypertension, immunosuppression, hyperglycemia and adrenal suppression (Hogeling, et al., 2011). The pulsed-dye laser has been proven effective for the treatment of superficial hemangiomas, the superficial component of mixed hemangiomas and ulcerated hemangiomas. Efficacy is however limited by the depth of laser penetration. Several treatments may be necessary, and treatments have been associated with some risk of scarring (Rudolph, 2003). Other, less common treatments include: cryotherapy, other forms of laser surgery, embolization, and use of chemotherapeutic agents, such as vincristine and cyclophosphamide. Other forms of laser surgery have included the argon laser for hemangiomas, the Nd:YAG (neodymium: yttrium-aluminum-garnet) laser for deeper lesions, and carbon dioxide laser for lesions such as subglottic hemangiomas. Some of these devices have been associated with significant scarring. Surgical excision may be recommended for hemangioma lesions that are sharply demarcated and pedunculated, are ulcerated and bleeding, have not responded to other modalities of treatment, and those that threaten function (Rudolph, 2003).

Oral Propranolol: Oral propranolol is being investigated as a treatment for infantile hemangioma, as both a first- and second-line treatment. This type of treatment is aimed primarily at lesions that interfere or have potential to interfere with vital function and/or are life-threatening (Drolet, et al., 2013). In some cases treatment may be recommended to improve cosmesis when there is risk of permanent disfigurement (Drolet, 2013).

Propranolol, a non-selective beta-blocker, exerts a vasoconstricting effect which may result in a change in color, reduction of lesion volume, softening and regression of the lesion. Induction of apoptosis is also a possible mechanism of action for reducing hemanigoma lesions. Initiation of therapy may be performed in a hospital setting as either inpatient or outpatient depending on the resources available for safe monitoring. Although specific dosing, age for initiation of therapy, duration of treatment, and expected clinical outcomes are not firmly established, treatment protocols have been published

Evidence evaluating the use of propranolol as a treatment for infantile hemangioma is primarily in the form of case reports, retrospective or prospective case series, and uncontrolled comparative trials involving small populations. Published randomized and/ or controlled trials are lacking but are currently being conducted through the U.S. National Institute of Health to evaluate safety and efficacy. Published data indicate the type of hemangioma lesion most often treated is a clinically compromising lesion, such as orbital or airway lesion. Age for initiation of therapy has ranged from one month to five years although most subjects were less than 12 months of age. Reported efficacy is variable but tends to be higher when administered during infancy and the proliferative phase of involution, although regression of lesions has been documented when administered during the involution phase. Duration of therapy within these trials ranged from one to 12 months with six months being the average. Follow-up evaluation of clinical outcomes varied as well, ranging from immediately following initial treatment to 18 months post-treatment.

Clinical effectiveness has been demonstrated as early as 24 hours following administration with reduction of volume, change in color from red to purple, and softening of the lesion (Leaute-Labreze, et al., 2011; Manunza, et al., 2010; Sans, et al., 2009). Complete regression in as little as two months following treatment has been reported (Sans, et al., 2009) and a majority of the published evidence demonstrates positive response rates with partial to complete regression of lesions and minor side effects (Léauté-Labrèze, et al., 2013; Luo, et al., 2014; Sharma, et al., 2013; Vassallo, et al., 2013; Hermans, et al., 2012; Ming-ming, et al., 2012; El-Essawy, et al., 2011; Spiteri Cornish and Reddy, 2011; Thoumazet, et al., 2011; Hogeling, et sl., 2011; Price, et al., 2011; Schupp, et al., 2011; Leaute-Labreze, et al., 2011; Al Dhaybi, et al., 2011; Manunza, et al., 2010; Buckmiller, et al., 2010; Sans, et al., 2009). In addition to regression of the lesions, improved clinical outcomes such as decrease in astigmatism, improved ambylopia (Vassallo, et al.,2013) and decreased airway obstruction (Hermans, et al., 2012) have been reported.

Peridis et al. (2011) published a meta-analysis on the effectiveness of propranolol for the treatment of infantile airway hemangioma and compared propranolol with other therapies. Included in this review was a statistical analysis of variables using an odds ratio and sensitivity analysis. Thirteen studies met inclusion criteria involving 36 subjects in total. The authors reported propranolol was an effective treatment for resolution of lesions ($P<0.00001$), and was significantly more effective than steroids ($P=0.0002$), CO_2 laser ($P=0.0005$), and vincristine (P0.01). It was noted propranolol decreased airway stenosis after one week of therapy from an average of 77.57% to 38.3% and after 4 weeks to an average of 24.6%. Only one child developed complications related to propranolol which was bronchoconstriction during the first week of therapy. Although the meta-analysis is limited by the strength of evidence reviewed which included case reports, case series, and observational studies, the results demonstrate propranolol is an effective treatment for infantile airway hemangioma.

Another meta-analysis published by Izadpanah et al. (2013) compared propranolol and corticosteroid use for treatment of hemangioma lesions. The analysis included 41 studies in total, involving 3424 subjects. Lesions were located on the trunk, extremities, head, neck and/or airway. A total of 2629 subjects received corticosteroids (oral or intralesional) and 795 received propranolol. Overall efficacy (regression of the lesion) for corticosteroid use was 69.1%, 17.6% developed side effects, rate of resolution was 84.5% receiving systemic and 66.4% receiving local administration. In comparison, the overall efficacy rate for propranolol was 97.3%, 13.7% developed side effects and rate of resolution was 98.9%. The response rate between propranolol and systemic corticosteroid use was statistically significant when intralesional studies were omitted, 97% versus 71% respectively. While the results of the meta-analysis are promising, the authors acknowledged it is limited by the lack of randomized controlled trials.

The American Academy of Pediatrics (AAP) conducted a comprehensive review of the literature involving a multidisciplinary team and published recommendations for use of propanolol as a treatment for infantile hemangiomas (Drolet, et al., 2013). With regards to treatment of infantile hemangioma, the following recommendations were made:

- treatment should be considered in the presence of ulceration, impairment of a vital function (ocular compromise or airway obstruction) or risk of permanent disfigurement
- screening for risks associated with propranolol use (heart rate, blood pressure, cardiovascular and pulmonary assessment) including ongoing monitoring following initiation of therapy
- target dose of 1-3mg/kg per day, divided into dosing three times daily at least 6 hours apart
- inpatient hospitalization for infants age 8 weeks or less, any age infant with inadequate social support or any age infant with comorbid conditions involving cardiovascular, respiratory or blood glucose status
- outpatient initiation with monitoring for infants and toddlers older than 8 weeks of age with adequate social support and without significant comorbid conditions
- data supporting the utility of Holter monitoring in infants after initiating therapy is lacking and the AAP has not reached consensus regarding its use

Randomized controlled trials comparing oral propranolol to standard therapies for treatment of cutaneous hemangiomas are limited and dosing strategies have not been firmly established. Nonetheless, there is some evidence in the form of observation studies to support clinical efficacy for regression of lesions and improved health outcomes. Additionally, as a result of widespread adoption of propranolol for infantile hemangioma, the AAP published consensus recommendations for initiation and use of propanolol, further supporting its use until the results of large-scale phase II/III trials are available. Based on the available evidence and acceptance in the medical community, and despite the need for randomized controlled trials, there is support of clinical efficacy for oral propranolol as a treatment for infants with complicated hemangiomas.

Port Wine Stain
Port wine stains are a type of vascular malformation involving the superficial capillaries of the skin. They vary in size and location and are usually present at birth although not always clinically evident. In rare cases, a port wine stain may be referred to as “acquired” and become evident after injury to the skin or in association with hormonal influences (Legiehn, Heran, 2008). Most often, lesions are found on the face, neck, arms or legs. They may be related to other underlying conditions, such as Sturge-Weber syndrome. Sturge-Weber syndrome, also known as encephalotrigeminal angiomatosis, is characterized by a facial port wine stain in a trigeminal V1 (i.e., ophthalmic) distribution, leptomeninigeal angiomatosis, and choroidal vascular malformation of the eye, which can lead to ipsilateral glaucoma and buphthalmos. Glaucoma occurs in 30% of patients with Sturge-Weber syndrome, and it develops before two years of age in 60% of these patients (Hussain, et al., 2004).

Port wine stains appear as sharply demarcated pink-red patches that darken with time and do not proliferate; growth of the lesion is dependent upon growth of the child. As the child matures, the lesion may become raised and exhibit red-to-purple nodules and papules in adult years, leading to potential disfigurement (e.g., pebbly and slightly thickened surfaces), and bleeding with trauma. Hypertrophy may develop in the soft tissue underlying the port wine stain. Early treatment may prevent the progression of development to hypertrophy and nodules in later years. It has been noted port wine stain lesions on the forehead or eyelids can be associated with ocular disorders and warrant frequent ophthalmology exams to prevent damage to the eye.

Laser devices such as the argon, carbon dioxide (CO_2), Nd:YAG, and copper vapor laser have been used to treat port wine stains. In many cases, these laser devices have been associated with poor cosmetic outcomes (Rothfleisch, et al., 2002). Pulsed dye laser therapy has been shown to be the most effective treatment for port wine stains; is associated with less adverse effects, including less post-operative scarring; and is considered the standard treatment of choice (Tucci, et al., 2009; Yang, et al., 2005; Schmults, 2005). Evidence in the published medical literature suggests efficacy is increased if lesions are treated in infancy, although size and location are also predictors of outcome (Conlon, Drolet, 2004). Nonetheless, while most port wine stains lighten after a series of pulsed dye laser treatments, some cannot be completely removed (Yang, et al., 2005).

Other Vascular Lesions/Malformations
Lymphatic (Lymphangioma): Lymphatic malformations consist of abnormally dilated lymphatic channels and commonly affect the head and neck area in children (lypmhagioma). Most are present at birth although some may appear later in childhood as a result of infection or trauma. These lesions are either macrocystic or microcystic; microcystic are more difficult to treat and more often associated with complications. Aside from cosmetic concerns, depending on the size and location of the mass the lesion may be symptomatic. For example, when the oral and pharyngeal mucosa is involved there may be tongue swelling, tongue hypertrophy, mucosal bleeding, speech difficulty, and airway compromise. Common complications include disfigurement,

infection and bleeding. Treatment is aimed at improving cosmesis, and alleviating any associated symptoms and involves surgical excision and/or sclerotherapy (Wetmore, Potsic, 2010; Tucci, et al, 2009; Morelli, 2011; Freiden, et al., 1997). Although used less frequently, other types of treatment such as scleroembolization and CO_2 laser have also been effective.

Arteriovenous: Arteriovenous malformations (AVM) of the skin are rare; however this type of lesion is a direct connection of artery to vein, bypassing the capillary bed. AVMs may appear at any time from birth to early adulthood and often remain stable for several years. They usually become noticeable at times of hormonal changes and at times may suddenly enlarge following infection or trauma (Tucci, et al., 2009). If the lesions are asymptomatic treatment is not necessary, however if ulceration and/or bleeding develop treatment is warranted and consists of embolization and excision (Wetmore, Potsic, 2010).

Venous: Venous malformations include but are not limited to vein only malformations and angiokeratomas. These lesions vary in size and may be superficial, deep or a combination of both. The lesions grow as the child grows but have a tendency to enlarge after direct trauma or with hormonal change such as during puberty or pregnancy from progressive ectasia of the vascular structure (Tucci, et al., 2009). For most lesions treatment is not necessary. When treatment is warranted, such as with pain from enlargement, treatment for superficial nodular lesions is surgical excision; larger deeper lesions may be treated with sclerotherapy. Other treatment modalities include ND:Yag laser therapy, endovenous laser therapy. In some instances treatments are combined to increase effectiveness however smaller localized lesions are usually managed with a single modality (Huang, Liang, 2010). Angiokeratomas are characterized by ectasia of the superficial dermal vessels with hyperkeratosis of the overlying dermal layer (Freiden, et al., 1997). They appear as flat hemangiomas with an irregular surface, with surgical excision being the treatment of choice (Wetmore, Potsic, 2010). Although angiokeratomas are generally asymptomatic bleeding and itching may occur with trauma.

U.S. Food and Drug Administration (FDA)
Lasers are regulated by the FDA as Class II devices and receive approval through the 510(k) process. According to the FDA, pulsed dye lasers are indicated for use in the treatment of cutaneous vascular lesions such as port wine stains and hemangiomas, and benign cutaneous lesions such as warts, striae and some forms of psoriasis.

Professional Societies/Organizations
The American Academy of Dermatology (AAD) published a guideline of care for hemangiomas of infancy (Freiden, et al., 1997). Although the guideline has not been modified since the initial publication, according to the AAD guideline, treatment of hemangiomas is dependent upon the size, location and severity of the tumor, the age of the patient, and the rate of involution. The guidelines support treatment for the following conditions:

- hemangiomas affecting vision, laryngeal involvement, nasal and auditory canal obstruction, Kasabach-Merritt syndrome, hepatic hemangiomatosis, cardiac failure, and skin ulceration
- hemangiomas that are likely to be disfiguring (e.g., located on the nose, lips, ear)
- hemangiomas that are very large with prominent dermal component, with or without subcutaneous component (e.g., facial hemangiomas)
- pedunculated hemangiomas

Use Outside of the US: The National Institute for Health and Care Excellence (NICE) published a procedural guidance document regarding intralesional photocoagulation of subcutaneous congenital vascular disorders and noted that due to inadequate evidence supporting safety and efficacy the procedure should not be used without special arrangements for consent, audit or research (NICE, 2004). Guidance for laser and other modalities of treatment were not found.

Summary
Cutaneous congenital hemangiomas, port wine stains and other vascular malformations such as venous and arteriovenous, or lymphangioma, can result in an undesired appearance. Elective treatment in such cases is often aimed at improving the individual's appearance, and is considered cosmetic. However, these lesions can also require medically appropriate treatment when they cause problems such as ulceration, bleeding, and recurrent infections, or when they are located in areas that can compromise function of vital structures such as

eyes, ears, or vocal cords. In such circumstances laser therapy and/or embolization therapy has been proven safe and effective.

There is also evidence in the published peer-reviewed scientific literature to suggest oral propranolol for the treatment of complicated infantile hemangiomas has been effective for regression of lesions and improved health outcomes. Although randomized controlled trials comparing oral propranolol with other therapies are lacking, recommendations from the American Academy of Pediatrics does support clinical efficacy for a subset of infants with complicated hemangiomas.

Coding/Billing Information

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

Hemangiomas and Other Venous Malformations

Covered when medically necessary for the treatment of a cutaneous and/or deep tissue hemangioma or other vascular lesion (i.e., venous, arteriovenous, lymphatic):

CPT* Codes	Description
17106	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); less than 10 sq cm
17107	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); 10.0 to 50.0 sq cm
17108	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); over 50.0 sq cm
37241	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicoceles)
37242	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; arterial, other than hemorrhage or tumor (eg, congenital or acquired arterial malformations, arteriovenous malformations, arteriovenous fistulas, aneurysms, pseudoaneurysms)
61626	Transcatheter permanent occlusion or embolization (eg, for tumor destruction, to achieve hemostasis, to occlude a vascular malformation), percutaneous, any method; non-central nervous system, head or neck (extracranial, brachiocephalic branch)

Covered when medically necessary when used to represent oral propranolol administration to an infant in the inpatient setting:

HCPCS Codes	Description
J8499	Prescription drug, oral, nonchemotherapeutic, NOS

ICD-9-CM Diagnosis Codes	Description
228.01	Hemangioma of skin and subcutaneous tissue

Port Wine Stains

Covered when medically necessary for the treatment of port wine stain:

CPT* Codes	Description
17106	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); less than 10 sq cm
17107	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); 10.0 to 50.0 sq cm
17108	Destruction of cutaneous vascular proliferative lesions (eg, laser technique); over 50.0 sq cm

ICD-9-CM Diagnosis Codes	Description
757.32	Congenital vascular hamartomas

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