



CIGNA MEDICAL COVERAGE POLICY

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Subject Photodynamic Therapy for Dermatologic Conditions

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Coverage Policy

CIGNA covers photodynamic therapy (PDT) using an appropriate light source with a topical photosensitizer (i.e., 5-aminolevulinic acid [5-ALA], methyl aminolevulinate [MAL]) as medically necessary for the treatment of nonhyperkeratotic actinic keratoses (AKs).

CIGNA covers photodynamic therapy (PDT) using an appropriate light source with a topical photosensitizer (i.e., 5-aminolevulinic acid [5-ALA], methyl aminolevulinate [MAL]) as medically necessary for the treatment of EITHER of the following conditions after failure, contraindication, or intolerance of standard medical/surgical care:

- superficial basal cell carcinoma
- Bowen's disease

CIGNA does not cover photodynamic therapy (PDT) for the treatment of ANY of the following dermatologic conditions because such therapy is considered experimental, investigational or unproven for these indications (this list may not be all-inclusive):

- acne vulgaris
- hyperkeratotic lesions
- nodular basal cell carcinoma
- psoriasis
- squamous cell carcinoma

- warts

CIGNA does not cover photodynamic therapy (PDT) for the treatment of ANY of the following indications as it is considered cosmetic in nature and not medically necessary (this list may not be all-inclusive):

- photoaging (i.e., photodamage or dermatoheliosis)
 - sebaceous gland hyperplasia
 - hirsutism
-

General Background

Photodynamic therapy (PDT), also referred to as photoradiation or photosensitizing therapy, is a two-step drug and light therapy procedure used to induce selective damage to defined tissue. The process starts with the application of a topical photosensitizer like the heme precursor 5-aminolevulinic acid (5-ALA) or its methyl ester, methyl aminolevulinate (MAL). Due to its low lipophilicity, ALA diffuses slowly through the cell membrane, therefore requiring that a large amount of ALA be applied to the diseased tissue. MAL is proposed to increase the diffusion rate and enter diseased tissue more rapidly and deeper, enhancing the production of protoporphyrin IX (PpIX), a potent photosensitizer, in the cells (Gold and Nestor, 2006; Angell-Petersen, et al., 2005). After a 3- to 48-hour application interval, the lesion is exposed to the appropriate light source. The medication, which has passed through the abnormal keratin overlying the lesion, is metabolized by the underlying cells and causes damage to the treated cells upon light exposure. Topical PDT has been introduced as a method of selectively destroying cells without harming surrounding normal tissue. The diseased cells have a tendency to accumulate more of the agent than normal tissue. The photosensitizer does not penetrate thicker lesions effectively and thus is not efficiently converted to PpIX. There are two light sources, blue light and red light. Red lights generally have a deeper level of penetration. Standard therapeutic wavelengths, fluence rates and intensity rates for light therapy for PDT have not yet been established.

U.S. Food and Drug Administration (FDA)

In December 1999, the FDA approved Levulan[®] Kerastick[®] (DUSA Pharmaceuticals, Inc., Valhalla, NY) for Topical Solution (aminolevulinic acid hydrochloride [HCl]), along with the light source BLU-U[®] Blue Light Photodynamic Therapy Illuminator (DUSA Pharmaceuticals, Inc., Valhalla, NY) for the treatment of nonhyperkeratotic actinic keratosis (AK) of the face or scalp.

Topical Metvixia[™] (methyl aminolevulinate) cream 16.8% in conjunction with the red light device CureLight Broadband Model CureLight 01 (PhotoCure ASA, Oslo, Norway) (PhotoCure ASA, Oslo, Norway) was approved by the FDA in July 2004, for the treatment of nonhyperkeratotic AK of the face and scalp. The approval was later updated to allow the use of the PhotoCure Aktelite[®] CL128 red light device (FDA, 2008).

Actinic Keratosis (AK)

AK, or solar keratosis, is a pre-cancerous condition that develops from overexposure to the sun and appears as small, reddish or natural colored rough, scaly spots that occur on the face, ears, and back of the hands. AK represents early epithelial transformation and may evolve into squamous cell carcinoma. Treatment options include topical agents such as fluorouracil or imiquimod, cryosurgery, electrodesiccation and curettage, dermabrasion, shave excision, and carbon dioxide laser. PDT is also an established treatment modality for the treatment of nonhyperkeratotic AK. The method of treatment of AK is dependent upon location, type, and size of the lesion and whether it is a primary or recurrent lesion (American Cancer Society [ACS], 2010; National Cancer Institute [NCI], 2010). PDT is not effective for the treatment of hyperkeratotic lesions. There is ineffective penetration of the photosensitizer in the thicker lesions and the consequent lack of conversion to PpIX.

Literature Review-Actinic Keratosis

Aminolevulinic Acid (ALA): The evidence in systematic reviews (Fayter, et al., 2010), and randomized controlled trials (Ritter, et al., 2010; Sotiriou, et al., 2009; Tschen, 2006; Piacquadio, et al., 2004; Jeffes, et al., 2001; Kurwa, et al., 1999) supports the treatment of nonhyperkeratotic AKs with ALA-PDT and blue light, especially for head and neck lesions, and is generally well-tolerated.

Methyl Aminolevulinatate (MAL): The safety and effectiveness of MAL-PDT for the treatment of nonhyperkeratotic AK lesions is supported by the evidence in systematic reviews (Fayter, et al., 2010) and randomized controlled trials (Kaufmann, et al., 2008; Pariser, et al., 2008; Wennberg, et al., 2008; Morton, et al., Nov. 2006; Freeman, et al., 2003; Pariser, et al., 2003). Lesions were located on the face, scalp, neck, trunk and extremities Overall, better outcomes and fewer adverse events were reported with MAL-PDT compared to treatment with cryotherapy.

Professional Societies/Organizations: In their guidelines for topical PDT, the British Association of Dermatologists (Morton, et al., 2008) stated that PDT “is an effective therapy for thin and moderate thickness AK, with superiority to cryotherapy depending on protocol. Efficacy is relatively poorer for acral lesions, but PDT may still offer therapeutic benefit”. Although showing lower efficacy in immunocompetent individuals, PDT may be a useful therapy in the treatment of epidermal dysplasia in organ transplant recipients. The BAD’s guidelines (de Berker, et al., 2007) on the management of AK stated that PDT was effective in 91% of clinical trials in which PDT was compared to cryotherapy. PDT may be “particularly good” in the treatment of superficial, multiple, and confluent AKs at sites of poor healing. PDT is probably best reserved for the treatment of extensive AKs not controlled with the other therapies.

Photodynamic guidelines developed in 2007 by the International Society for Photodynamic Therapy in Dermatology stated that PDT is “highly effective” for the treatment of AK, offering the advantage of “excellent cosmetic outcome” (Braathen, et al., 2007).

The National Comprehensive Cancer Network® (NCCN®) (2010) stated that AK should be treated aggressively upon diagnosis and listed PDT as an accepted treatment option.

According to the National Institute for Clinical Excellence (NICE) (2006) (United Kingdom), the evidence is adequate to support the efficacy of PDT for the treatment of AK, but that PDT may be more appropriate for large, superficial lesions rather than deep tumors.

Basal Cell Carcinoma (BCC)

BCC is the most common type of skin cancer in humans. There are several different clinical presentations of BCC, but the most common are superficial BCC and nodular BCC. Superficial BCC lesions appear as a scaly patch or pin/red papule with a threadlike border, most often on the trunk, and are typically slow growing and noninvasive. The hallmark of nodular BCC is a waxy, translucent or pearly appearance with telangiectatic vessels. It appears as a nodular or nodular ulcerative lesion with raised borders looking like a sore that often bleeds, heals and recurs again. The type of treatment provided will depend upon the characteristics of the tumor. The first line treatment is typically surgical excision which has the highest success rates. According to the National Cancer Institute (NCI), Mohs surgery has the highest five-year cure rate for primary and recurrent tumors. Other traditional treatment options include topical creams such as fluorouracil or imiquimod, cryosurgery, radiation therapy, electrodesiccation and curettage (Ramsey and Sewell, 2010; NCI, 2008; Bath-Hextall, et al. 2007). PDT is an established treatment option for superficial basal cell carcinoma.

Literature Review: Although there are a limited number of studies evaluating the efficacy of PDT for the treatment of superficial BCC, PDT is an established method of therapy for superficial BCC that is unresponsive to conventional treatment methods or in cases when traditional therapies are contraindicated or not tolerated (Ramsey and Sewell, 2009; Szeimies, et al., 2008; Telfer, et al., 2008; Szeimies, 2007; Angell-Petersen, et al., 2006). However, the evidence in the peer-reviewed literature and professional societies does not support PDT for the treatment of nodular BCC. Nodular BCC studies have demonstrated various short-term response rates (59–92%) and recurrence rates (5–44%). Various protocols (e.g., formulations, concentration, light sources, penetration enhancers, ALA application time vs. light application) have been used. Several studies have included extemporaneously prepared ALA. There is a lack of long-term results regarding the efficacy of PDT for the treatment of nodular BCC (Rao, 2010; Braathen, et al., 2007).

Fayter et al. (2010) conducted a systematic review of randomized and nonrandomized clinical trials investigating PDT for the treatment of various cancerous and precancerous conditions. The review of 88 studies included two randomized controlled trial (n=131 patients) comparing PDT to placebo, three randomized controlled trials comparing PDT to surgical excision (n=283 patients, 331 lesions) and one randomized controlled trial comparing MAL-PDT to ALA-PDT (n=39 patients, 43 lesions) for the treatment of nodular BCC. The studies suggested that

PDT was superior to placebo but less effective than surgical excision. Cosmetic outcomes were more favorable following PDT. Due to the small patient populations and the poor quality of the studies, PDT could not be recommended as a treatment option for this condition.

Foley et al. (2009) reported on two multicenter randomized controlled trials comparing MAL-PDT (n=66 patients, 75 lesions) to placebo-PDT (n=65 patients, 79 lesions) for the treatment of nodular BCC. One study was conducted in the United States (n=65 patients, 79 lesions) and one in Australia (n=66 patients, 81 lesions). Both studies used the same design and procedures. Of the 64 MAL-treated patients with information available, 48 had received at least one form of previous therapy. All patients initially received two PDT sessions separated by a one-week interval. Follow-ups occurred at three and six months. Partial response lesions were retreated at three months and followed up at six and nine months. Lesions with no response or progression at three months and lesions with an incomplete response at six months after a second treatment were excised. Overall, histologically verified lesion complete response rates were "superior" following MAL-PDT compared to placebo PDT (73% vs. 27%, respectively). Lesion complete response rates for MAL-PDT and placebo-PDT were 78% vs. 33% in the United States study and 68% vs. 19% in the Australian study, respectively. Cosmetic outcomes were rated as "good to excellent" in 98% of the evaluable, completely responding MAL-treated lesions. Facial lesions and smaller lesions responded better. Twenty lesions in the MAL group did not show a complete response rate. More adverse events were reported in the MAL group compared to the placebo group (91% vs. 66%, respectively). Limitations of the study include the small patient population and short-term follow-up.

In a randomized controlled trial, Mosterd et al. (2008) compared the efficacy of ALA-PDT to surgical excision (SE) of nodular basal cell carcinoma (nBCC) (n=149 patients/173 lesions). PDT patients, previously untreated, underwent tumor debulking three weeks prior to PDT and were illuminated twice on the same day, 60 minutes apart during the PDT treatment. Mean follow-up was 28 months (range 0-57 months). Three months following treatment, 94% of the ALA-PDT group had completely resolved compared to 98% of the SE group (p=0.27). There were two failures in the SE group and 21 in the PDT group. Intention-to-treat analyses on a three-year analysis reported that the cumulative incidence of failure for SE was 2.3% compared to 30.3% for PDT (p<0.001). The study showed that PDT is inferior to surgical excision in the treatment of nodular basal cell carcinoma.

Smucler et al. (2008) prospectively studied the ability of PDT-ALA alone, Erbium (Er):YAG laser alone and PDT plus Er:YAG to ablate nBCC tumors in the head and neck regions. Subjects (n=286) had recurring nodular BCC refractory to previous intervention (i.e., surgical excision, cryotherapy, laser ablation). Follow-up occurred at three, six and 12 months. Each patient was treated with all three methods. The lesions treated with PDT/Er:YAG were treated first with Er:YAG to reduce the tumor depth making the tumor more responsive to PDT. At the three-month follow-up, percentages without recurrence were 99.1% for PDT only, 98.39% for Er:YAG only and 100% for the PDT/Er:YAG group. At the end of a year, the percentage of patients without recurrence following PDT only was 94.85%, 91.75% for Er:YAG, and 98.97% for PDT/Er:YAG. Combined therapy was significantly more effective than PDT alone (p<0.01). Recurrence occurred more quickly following Er:YAG and a noticeable fall was noted in effectiveness between month 6 and 12 (98.11% to 94.85%) following PDT only. There was significantly better healing following Er:YAG compared to PDT (p<0.01), and at 12 months, patient preference was for Er:YAG only (67.5%). Based on the results of this study the authors did not recommend the use of PDT only as a treatment modality for nodular BCC.

Bath-Hextall et al. (2007) conducted a review of 27 randomized controlled trials, 18 published studies and nine abstracts related to the treatment of BCC with imiquimod (n=9), intralesional interferon (n=4), BEC-5 cream (n=1), fluorouracil (n=2), surgery (n=3), radiotherapy (n=2), cryotherapy (n=4), and PDT (n=8). The authors noted that surgery revealed the lowest failure rates with radiotherapy and surgery appearing to be the most effective treatment modalities. PDT yielded better cosmetic outcomes than surgery, but there were high failure rates with PDT compared to surgery, radiotherapy and cryotherapy. The majority of studies included only low-risk BCC, and there is a need for long-term follow-up data regarding the effectiveness of PDT. Overall, there has been "very little good quality research on the efficacy of treatment modalities" for BCC. Few treatments have been compared to surgery.

Rhodes et al. (2007) conducted a multicenter, prospective, randomized controlled trial to assess the recurrence rate of primary nodular BCC lesions following treatment with MAL-PDT (n=50 patients/53 lesions) compared to simple excisional surgery (n=47 patients/52 lesions). At the end of three months, 49 PDT-treated lesions (46

patients) and 52 surgically-treated lesions (47 patients) demonstrated complete response and were enrolled for a five-year follow-up. The MAL-group experienced two recurrent lesions compared to one recurrent lesion in the surgical group between years two and three. Thirty-one MAL-treated patients and 35 surgically-treated patients were available for the five-year follow-up. The five-year MAL recurrence rate was 14% compared to 4% for the surgical group. The five-year estimated sustained complete response rate was 76% for the MAL group compared to 96% for the surgical group ($p=0.01$). Cosmesis was better in the PDT group (87% vs. 54%) ($p=0.007$).

Kuijpers et al. (2006) compared the effectiveness of PDT with 5-ALA ($n=22$) to PDT with MAL ($n=21$) for the treatment of nodular BCC. Patients were randomly assigned, and results were reported at eight weeks following therapy. The authors reported no differences in the outcomes and stated that ALA and MAL were equally recommended. Rhodes et al. (2004) conducted a multicenter, randomized, prospective trial to compare MAL-PDT with standard excision surgery for nodular BCC ($n=97$ patients/105 lesions). Complete response rates did not differ significantly between the two groups. At 12 months, tumor-free rates were higher in the surgery group (96%) than in the MAL-PDT group (83%). At 24 months, five lesions reoccurred after MAL-PDT and only one after surgery.

Professional Societies/Organizations: The National Comprehensive Cancer Network (2010) stated that “PDT may be a treatment option in patients with low-risk, superficial basal cell skin cancer, where surgery or radiation is contraindicated or impractical, even though the cure rate may be lower”.

In their 2008 guidelines on the management of BCC, The British Association of Dermatologists (BAD) included the use of PDT as a treatment option for BCC. They stated that PDT is a good treatment for primary superficial BCC and a “reasonable treatment for primary low-risk” nBCC (Telfer, 2008). In their guidelines for topical PDT, the BAD stated that MAL-PDT and ALA-PDT are effective treatments for BCC. MAL-PDT is effective in the treatment of nodular BCC, but it has a lower efficacy than surgical excision and may be an option when surgical excision is suboptimal (Morton, et al., 2008).

The NCI (2010) stated that Mohs surgery has the highest cure rate of all surgical treatments for BCC. Other treatment methods include simple excision, electrodesiccation and curettage, cryosurgery, radiation therapy, carbon dioxide laser, topical fluorouracil, interferon alpha. They stated that PDT may be a treatment option for patients with “superficial epithelial skin tumors”.

The International Society for Photodynamic Therapy in Dermatology (Braathen, et al., 2007) recommended PDT for the treatment of superficial BCC as a reliable and effective method, yielding excellent or good cosmetic outcomes and offers an advantage in the treatment of large, extensive, and multiple lesions. Studies of MAL-PDT have demonstrated long-term efficacy (five-year follow-up) for the treatment of superficial and nodular BCC.

According to NICE (2006), the level of evidence is adequate to support the efficacy of PDT for the treatment of BCC.

Bowen’s Disease

Bowen’s disease, a superficial type of squamous cell carcinoma (SCC) that has not yet spread (i.e., SCC in situ), is considered the earliest form of SCC. It appears as a persistent red-brown, scaly patch which may resemble psoriasis or eczema. If untreated, it can invade deeper structures. Topical therapy, surgically excision, cryotherapy, and liquid nitrogen are treatment options for Bowen’s disease. PDT is an established treatment alternative for individuals who fail, cannot tolerate, or are not a candidate for conventional therapies.

Literature Review: The evidence reported in systematic reviews (Fayter, et al., 2010) and randomized controlled trials have concluded that PDT is an effective treatment modality for Bowen’s disease (Garcia-Zuazaga, et al., 2005; Morton, et. al, 2002; Salim, et al., 2003).

Professional Societies/Organizations: The NCCN (2010) stated that PDT may be a treatment option “in patients with low-risk, squamous cell carcinoma in situ (Bowen’s disease), where surgery or radiation is contraindicated or impractical, even though the cure rate may be lower”.

In a 2007 guideline for the management of Bowen's disease, the British Association of Dermatologists (BAD) stated that "PDT has been shown to be equivalent or superior to cryotherapy and 5-FU, either in efficacy and/or in healing." They explain that PDT may be especially beneficial in the treatment of large lesions on the lower leg and other difficult sites (Cox, et al., 2007). In their 2008 guidelines for PDT, BAD also stated that PDT is equivalent or superior to the use of topical 5-FU and offers "particular advantages for large/multiple patch disease and for lesions at poor healing sites" (Morton, et al., 2008).

Recommendations by the International Society for Photodynamic Therapy in Dermatology (Braathen, et al., 2007) stated that PDT is as effective as cryotherapy and topical fluorouracil with fewer adverse events and should be considered a first-line therapy. Surgery is recommended for nonresponders.

The NICE (2006) stated that the evidence supports the use of PDT for the treatment of Bowen's disease especially when there are multiple large, superficial lesions that would otherwise require extensive surgery.

Other Indications

There are numerous other proposed indications for the use of PDT in dermatologic conditions including but not limited to: acne vulgaris, squamous cell carcinoma, warts, and psoriasis. Studies have included small heterogeneous patient populations and mixed outcomes. Some studies reported intolerance to PDT due to pain, no improvement in the condition, and/or in some cases worsening of the condition. PDT is not an established treatment modality for these conditions, and the evidence in the published peer-reviewed literature does not support the safety and effectiveness of its use.

Acne Vulgaris: Acne vulgaris is a chronic, inflammatory disease of the pilosebaceous follicles characterized by the formation of open and closed comedones (i.e., whiteheads and blackheads), erythematous papules and pustules, pseudocysts and nodules. Treatment for this condition includes topical medications, systemic therapy with antibiotics, retinoids and hormonal medications, and/or in severe cases surgical intervention. There is insufficient evidence supporting the safety and efficacy of PDT for the treatment of acne.

A limited number of studies with small patient populations and short-term follow-up have reported various clinical improvement of acne lesions after treatment with PDT. Orringer et al. (2010) conducted a randomized controlled split-face trial (n=44) and compared the effects of 5-ALA PDT to no therapy for the treatment of acne vulgaris. The patients received up to three treatment sessions at 2-week intervals. Clinical evaluations included live lesion counts and global grading with a modified Leeds acne severity scale. Follow-ups occurred every two weeks for 16 weeks, and counts of papules, pustules, cysts, open comedones, closed comedones, and erythematous macules were recorded. At week ten, there was a statistically significant decrease in mean inflammatory papule count in the treated skin ($p=0.01$), but the effect was transient with no improvement at week 16. With one exception, compared to baseline there were no significant changes in lesion counts of any subtype in the treated and untreated skin ($p>0.05$). There was a significant improvement in the treated skin compared to the untreated skin in the mean Leeds scores ($p=0.01$). Eight (18%) patients were considered responders (i.e., 25% decrease in lesion count) and inflammatory lesions responded better than noninflammatory lesions. Few adverse events were reported. Based on the results of the study, the authors concluded that an improvement in acne with their PDT regimen was "modest and inconsistent".

A systematic review of the literature "to assess the effects of optical treatments for acne vulgaris" by Haedersdal et al. (2008a) included five randomized controlled trials that used ALA- or MAL-PDT (n=114) for the treatment of acne vulgaris. Outcomes included: significantly better results with two treatments of MAL-PDT compared to no treatment ($p=0.005$) and placebo-PDT ($p=0.0006$); three ALA-PDT treatments for back acne were significantly better than no treatment; efficacy and pain scores were comparable with ALA-PDT and MAL-PDT; and ALA-PDT resulted in more severe erythema, pustular eruptions and epithelial exfoliation. In a randomized controlled trial, Haedersdal et al. (2008b) compared the results of the treatment of acne vulgaris by long-pulsed dye laser (LPDL) to LPDL with MAL-PDT (n=15). Inflammatory lesions were reduced significantly more with MAL-LPDL compared to LPDL only ($p=0.004$), noninflammatory lesions reduced "similarly" in both treatments, and patients treated with MAL-LPDL were more satisfied ($p<0.001$).

Yeung et al. (2007) conducted a randomized controlled trial (n=30) to compare the effects of intense pulsed light (IPL) to IPL plus MAL-PDT for the treatment of skin types IV or V with more than 10 moderate acne lesions. The untreated side of the face served as the control. Twenty-five percent of subjects withdrew due to intolerance to

MAL. A mean significant improvement in the inflammatory lesions was not observed with either treatment compared to the control group, but there was a significant improvement in noninflammatory lesions with both therapies 12 weeks following treatment.

Horfelt et al. (2006) conducted a randomized controlled trial comparing MAL-PDT to placebo in 30 patients with moderate inflammatory facial acne. Treatments were randomized to either side of each patient's face. Based on results at 10-weeks' follow-up, the authors reported significant improvement with MAL and suggested that further studies be conducted. Wiegell and Wulf (April 2006) conducted a randomized trial using MAL compared to ALA for the treatment of inflammatory acne. At twelve weeks, there was no significant difference in the response of the lesions. However, they reported more prolonged and severe adverse effects with ALA-PDT. Another randomized trial by Wiegell and Wulf (May 2006) compared patients treated with MAL (n=19) to patients who received no treatment (n=12). A 68% reduction was noted in inflammatory lesions in the MAL group at 12 weeks compared to no improvement in the group that received no treatment.

The British Association of Dermatologists (Morton, et al., 2008) stated that although PDT can improve inflammatory acne, "optimization of protocols, to sustain response while minimizing adverse effects, is awaited".

Squamous Cell Carcinoma (SCC): SCC, the second most common form of skin cancer, is often nodular and erythematous and may include keratin plugs, horns or ulceration. Surgical removal and Mohs' micrographic surgery are indicated over other treatment methods because of the metastatic potential of these lesions. It is not unusual for repeat treatment to be necessary in order to completely eradicate the affected tissue. PDT is not an established treatment modality for SCC.

Morton et al. (2006) conducted a randomized trial comparing outcomes of the treatment of squamous cell carcinoma with MAL-PDT to cryotherapy and to topical fluorouracil. The trial included 40 patients from 11 European centers. At 12 months, results from MAL-PDT were "superior" to cryotherapy and better than fluorouracil. A 2006 randomized controlled trial on PDT and SCC was performed on 40 organ transplant recipients to determine the preventive effect of PDT on SCC. After one year, no statistically significant difference was found in the occurrence of SCC in the treated versus the untreated arm (de Graaf, et al., 2006).

In their 2007 guidelines for the use of PDT for dermatological conditions, the International Society for Photodynamic Therapy in Dermatology concluded that there was insufficient evidence to support the routine use of PDT for the treatment of SCC (Braathen, et al., 2007).

The British Association of Dermatologists (Morton, et al., 2008) stated that "the high efficacy of topical PDT for in situ SCC and the efficacy figures reported particularly for superficial invasive lesions limited to papillary dermis, suggest that depth of therapeutic effect is the limiting factor for PDT in invasive SCC, with further study required. Current evidence supports the potential of topical PDT for superficial, microinvasive SCC, but in view of its metastatic potential, topical PDT cannot currently be recommended for the treatment of invasive SCC".

Psoriasis: Psoriasis is a chronic, systemic inflammatory disease affecting multiple systems, including the skin. It is characterized by scaly, erythematous patches, papules and plaques. Depending on the severity of the disease, treatment may include topical creams, biologic agents, phototherapy, and/or photochemotherapy.

There is insufficient evidence in the published peer-reviewed literature to support the effectiveness of PDT for the treatment of psoriasis. In a randomized controlled trial (n=12) comparing various dosages, Schleyer et al. (2006) reported that ALA PDT was not an appropriate treatment for psoriasis because of the disappointing clinical efficacy.

The 2010 American Academy of Dermatology guidelines on the management of psoriasis do not include PDT as a treatment option for this condition.

In their guidelines for topical PDT, the British Association of Dermatology (Morton, et al., 2008) stated that the overall body of evidence does not support PDT for the treatment of psoriasis.

Warts: Warts are benign tumors involving the skin and epithelial tissues. They are classified by their clinical features (e.g., flat, filiform) and by the location (e.g., genital, plantar). Treatment depends on the type and location of the wart.

Evidence in the published peer-reviewed literature does not support the effectiveness of PDT for the treatment of warts. In a randomized controlled trial, Liang et al. (2009) evaluated the safety and efficacy of ALA-PDT (n=67) to CO₂ laser therapy (control group) (n=23) for the treatment of condylomata acuminata (CA). The number of warts per patient was 1.84 ± 0.82. Follow-up for patients (n=87) with complete clearance lasted for 12 weeks. In the ALA group, 95.93% of patients achieved complete clearance compared to 100% in the control group. A total of 75 warts (60.98%) achieved clearance after one PDT treatment, 25 warts (20.32%) after two treatment cycles, 18 warts (14.63%) after three treatment cycles and five warts (4.07%) did not clear. At the 12-weeks follow-up, a statistically significant recurrence rate was reported (p<0.05) with six recurrences occurred in the ALA group compared to four in the control group. The adverse reaction rate in the control group (100%) was significantly higher than the adverse reaction rate in the ALA group (8.82%) (p<0.05). Limitations of the study include the small patient population and short-term follow-up.

In a systematic review of the literature on topical treatments for cutaneous warts that included five PDT randomized controlled trials, Gibbs and Harvey (2006) concluded that the benefits and risks of the use of PDT for the treatment of warts remained to be determined.

The British Association of Dermatology (Morton, et al., 2008) guidelines on topical PDT stated that “studies continue to support the potential of topical PDT in viral warts, particularly plantar warts, but it appears a relatively painful therapy option, with outcomes dependent on adequate paring and the use of a keratolytic agent pre-PDT”.

Photoaging and Photodamage (Dematoheliosis): Photoaging, also called photodamage or dematoheliosis, refers to chronic cosmetic changes that occur over the course of time as the result of repeated exposure to the sun. This may include wrinkles, roughness, dark spots, leathery course skin, and telangiectasia which are untoward cosmetic changes (AAD, 2010). Photoaging is a benign condition; treatment is aimed at improving appearance and therefore, would not be considered medically necessary.

Sebaceous Gland Hyperplasia: Sebaceous glands are located in the skin, attached to hair follicles and produce an oily substance called sebum. They are found mainly on the face, neck, back and chest. Sebaceous gland hyperplasia appears as small white or yellow lesions or papules. A decrease in cellular turnover results in the accumulation of sebocytes within the sebaceous gland, causing an enlargement of the gland. Sebaceous gland hyperplasia is a benign condition and does not require treatment (Hogan, 2009; AAD, 2010).

Hirsutism: Hirsutism, hypertrichosis or excess hair, is the presence of coarse, dark hair where it does not typically grow (e.g., lip, chin, chest), especially in women. The goal of treatment using interventions such as PDT is cosmetic in nature and as such, would not be considered medically necessary.

Summary

Evidence in the published peer-reviewed scientific literature and professional societies support photodynamic therapy (PDT) for the treatment of nonhyperkeratotic actinic keratosis (AK). PDT is established as an alternative therapy for the treatment of superficial basal cell carcinoma and Bowen’s disease that is unresponsive to standard medical and/or surgical treatment or in individuals in whom standard therapy is contraindicated or cannot be tolerated.

PDT is proposed for the treatment of other dermatologic conditions, including acne vulgaris, nodular basal cell carcinoma, hyperkeratotic lesions, psoriasis, and warts. Well-designed randomized controlled trials with large patient populations and long-term follow-ups are needed to determine the role of PDT in these other conditions. Patient safety and treatment efficacy have not been established. Photoaging, sebaceous gland hyperplasia and hirsutism are benign conditions which result in untoward cosmetic effects. Treatment for these conditions is for the purpose of improving appearance and not medically necessary.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
96567	Photodynamic therapy by external application of light to destroy premalignant and/or malignant lesions of the skin and adjacent mucosa (eg, lip) by activation of photosensitive drug(s), each phototherapy exposure session

HCPCS Codes	Description
J7308	Aminolevulinic acid HCL for topical administration, 20%, single unit dosage form (354 mg)
J7309	Methyl aminolevulinate (MAL) for topical administration, 16.8% , 1 g

ICD-9-CM Diagnosis Codes	Description
173.0-173.9 [†]	Other malignant neoplasm of skin
232.0-232.9	Carcinoma in situ of skin, Bowen's disease
702.0 ^{††}	Actinic keratosis

[†]**Note:** Covered when medically necessary and used to report superficial basal cell carcinoma.

^{††}**Note:** Covered when medically necessary and used to report nonhyperkeratotic actinic keratosis.

Experimental/Investigational/Unproven/Cosmetic/Not Medically Necessary/Not Covered:

ICD-9-CM Diagnosis Codes	Description
078.10- 078.19	Viral warts
686.8	Other specified local infections of skin and subcutaneous tissue
686.9	Unspecified local infection of skin and subcutaneous tissue
696.1	Other Psoriasis
696.2	Parapsoriasis
701.0-701.9	Other hypertrophic and atrophic conditions of skin, hyperkeratotic lesions
702.11- 702.19	Seborrheic keratosis
702.8	Other specified dermatoses
704.1	Hirsutism
706.0	Acne Varioliformis
706.1	Acne vulgaris
706.2	Sebaceous cyst
706.9	Unspecified disease of sebaceous glands
709.1	Vascular disorders of skin
709.8	Other specified disorders of skin
709.9	Other dyschromia
782.1	Rash and other nonspecific skin eruption
	All other codes

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	2/15/2008	0033	Photodynamic Therapy for Dermatologic Conditions

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