

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

RELATED PROTOCOLS

Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus
Photodynamic Therapy for Choroidal Neovascularization

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| Individuals:  
• With nonhyperkeratotic actinic keratoses on the face or scalp  
Interventions of interest are:  
• Photodynamic therapy | Comparators of interest are:  
• Pharmacologic therapy  
• Cryotherapy  
• Laser therapy | Relevant outcomes include:  
• Symptoms  
• Change in disease status  
• Quality of life  
• Treatment-related morbidity |
| Individuals:  
• With nonhyperkeratotic actinic keratoses on the upper extremities  
Interventions of interest are:  
• Photodynamic therapy | Comparators of interest are:  
• Pharmacologic therapy  
• Cryotherapy  
• Laser therapy | Relevant outcomes include:  
• Symptoms  
• Change in disease status  
• Quality of life  
• Treatment-related morbidity |
| Individuals:  
• With low-risk basal cell carcinoma  
Interventions of interest are:  
• Photodynamic therapy | Comparators of interest are:  
• Pharmacologic therapy  
• Cryotherapy  
• Surgery  
• Radiotherapy | Relevant outcomes include:  
• Symptoms  
• Change in disease status  
• Quality of life  
• Treatment-related morbidity |
| Individuals:  
• With squamous cell carcinoma in situ  
Interventions of interest are:  
• Photodynamic therapy | Comparators of interest are:  
• Pharmacologic therapy  
• Cryotherapy  
• Surgery  
• Radiotherapy | Relevant outcomes include:  
• Symptoms  
• Change in disease status  
• Quality of life  
• Treatment-related morbidity |
Protocol Dermatologic Applications of Photodynamic Therapy

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**DESCRIPTION**

Photodynamic therapy (PDT) refers to light activation of a photosensitizer to generate highly reactive intermediaries, which ultimately cause tissue injury and necrosis. Photosensitizing agents are being proposed for use with dermatologic conditions such as actinic keratoses (AKs) and nonmelanoma skin cancers.

**SUMMARY OF EVIDENCE**

For individuals who have nonhyperkeratotic AKs on the face or scalp who receive PDT, the evidence includes meta-analyses and randomized controlled trials (RCTs). Relevant outcomes are symptoms, change in disease status, quality of life (QOL), and treatment-related morbidity. Evidence from multiple RCTs has found that PDT improves the net health outcome as measured by complete clinical clearance of lesions in patients with nonhyperkeratotic AKs on the face or scalp compared with placebo or other active interventions. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have nonhyperkeratotic AKs on the upper extremities who receive PDT, the evidence includes a systematic review and RCTs. Relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. A systematic review of interventions for nonface and nonscalp AKs found PDT to be superior to placebo for complete clearance but found a significant increase in complete clearance with cryotherapy versus PDT. In 2 placebo controlled RCTs, significantly more patients had a complete clearance of AKs with ALA/PDT with blue light compared to placebo at 12 weeks, and a third found a significantly greater reduction in mean lesion count at 4 weeks. Two small RCTs compared ALA/PDT using red light to imiquimod or 5-fluorouracil and found similar efficacy between the active treatment groups after 6 months of follow-up. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have low-risk basal cell carcinoma who receive PDT, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. Systematic reviews of RCTs have found that PDT may not be as effective as surgery for low-risk superficial and nodular basal cell carcinoma. In the small number of trials available, PDT was more effective than a placebo. The available evidence from RCTs has suggested that PDT has better cosmetic outcomes than surgery.
for low-risk basal cell carcinoma. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have squamous cell carcinoma in situ who receive PDT, the evidence includes a meta-analysis and RCTs. The relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. RCTs have found that PDT has similar or greater efficacy compared with cryotherapy and 5-fluorouracil. Additionally, adverse events and cosmetic outcomes appear to be better after PDT. Few RCTs have compared PDT with surgery or radiotherapy; as a result, conclusions cannot be drawn about PDT compared with these other standard treatments. Current guidance from the National Comprehensive Cancer Network notes that topical modalities, including PDT, may have lower cure rates than with surgical treatment. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have nonmetastatic invasive squamous cell carcinoma who receive PDT, the evidence includes observational studies and a systematic review of observational studies. The relevant outcomes are overall survival, symptoms, change in disease status, QOL, and treatment-related morbidity. Conclusions cannot be drawn from small, uncontrolled studies. RCTs are needed to determine the safety and efficacy of PDT for this condition. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have acne who receive PDT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. The available RCTs have not consistently found significantly better outcomes with PDT compared with other interventions, and meta-analyses did not find significantly better results with PDT versus placebo. Several trials have found that PDT is associated with high rates of adverse events leading to the cessation of treatment. Trials tended to have relatively small sample sizes and used a variety of comparison interventions. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have noncancerous dermatologic skin conditions (e.g., hidradenitis suppurativa, mycoses, port-wine stain) who receive PDT, the evidence includes case series, systematic reviews of uncontrolled series, and an RCT for port-wine stain. Relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. RCTs are needed to determine the safety and efficacy of PDT for these conditions. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

**POLICY**

Photodynamic therapy may be considered **medically necessary** as a treatment of:

- Non-hyperkeratotic actinic keratoses of the face and scalp (see Policy Guidelines).
- Non-hyperkeratotic actinic keratoses of the upper extremities (see Policy Guidelines).
- Low-risk (e.g., superficial and nodular) basal cell skin cancer only when surgery and radiation are contraindicated.
- Cutaneous squamous cell carcinoma in situ (Bowen disease) only when surgery and radiation are contraindicated.

Photodynamic therapy is considered **investigational** for other dermatologic applications, including, but not limited to, acne vulgaris, high-risk basal cell carcinomas, hidradenitis suppurativa, and mycoses.

Photodynamic therapy as a technique of skin rejuvenation, hair removal, or other cosmetic indications would be **cosmetic** and therefore is considered **not medically necessary**.
POLICY GUIDELINES

Surgery or radiation is the preferred treatment for low-risk basal cell cancer and Bowen’s disease. If photodynamic therapy is selected for these indications because of contraindications to surgery or radiation, patients and physicians need to be aware that it may have a lower cure rate in comparison with surgery or radiation.

Photodynamic therapy typically involves two office visits: one to apply the topical aminolevulinic acid and a second visit to expose the patient to the blue light. The second physician office visit, performed solely to administer blue light, should not warrant a separate Evaluation and Management service. Photodynamic protocols typically involve two treatments spaced a week apart; more than one treatment series may be required.

Based on characteristics of patients enrolled in randomized controlled trials, four or more lesions per site (face, scalp, or upper extremities) is an appropriate threshold for use of photodynamic therapy for patients with non-hyperkeratotic actinic keratosis.

MEDICARE ADVANTAGE

For Medicare Advantage it is medically necessary to destroy actinic keratoses by, but not limited to, cryosurgery with liquid nitrogen, curettage, excision, and photodynamic therapy, based on what the physician determines is the best treatment for the patient and the characteristics of the lesions present.

BACKGROUND

PHOTODYNAMIC THERAPY

Photodynamic therapy (PDT) refers to light activation of a photosensitizer to generate highly reactive intermediaries, which ultimately cause tissue injury and necrosis. Two common photosensitizing agents are 5-aminolevulinic acid (ALA) and its methyl ester, methyl amino levulinate. When applied topically, these agents pass readily through abnormal keratin overlying the lesion and accumulate preferentially in dysplastic cells. The agents ALA and methyl amino levulinate are metabolized by underlying cells to photosensitizing concentrations of porphyrins. Subsequent exposure to photoactivation (maximum absorption at 404 to 420 nm and 635 nm) generates reactive oxygen species that are cytotoxic, ultimately destroying the lesion. PDT can cause erythema, burning, and pain. Healing occurs within 10 to 14 days, with generally acceptable cosmetic results. PDT with topical ALA has been investigated primarily as a treatment of actinic keratoses (AKs).

REGULATORY STATUS

In 1999, Levulan® Kerastick™, a topical preparation of ALA, in conjunction with illumination with the BLU-U™ Blue Light Photodynamic Therapy Illuminator, was approved by the U.S. Food and Drug Administration (FDA) for the treatment of nonhyperkeratotic AKs of the face and scalp. In 2018, the indication was expanded to include nonhyperkeratotic AKs of the upper extremities. The product is applied in the physician’s office.

FDA product code: MVF.

In 2016, the FDA approved Ameluz® (aminolevulinic acid hydrochloride) gel, 10% (BF-200 ALA; Biofrontera AG) in combination with PDT using BF-RhodoLED lamp, to be used for the lesion-directed and field-directed treatment of AKs of mild-to-moderate severity on the face and scalp. The treatment is to be administered by a healthcare provider.

A ALApatch technology is available outside of the U.S. through an agreement between Intendis (now Bayer HealthCare) and Photonamic. The ALA patch is not approved by the FDA.
Another variant of PDT for skin lesions is Metvixia® used with the Aktilite CL128 lamp, each of which received the FDA approval in 2004. Metvixia® (Galderma; Photocure) consists of the topical application of methyl amino levulinate (in contrast to ALA used in the Kerastick procedure), followed by exposure with the Aktilite CL128 lamp, a red light source (in contrast to the blue light source in the Kerastick procedure). Broadband light sources (containing the appropriate wavelengths), intense pulsed light (FDA product code: ONF), pulsed dye lasers, and potassium-titanyl-phosphate lasers have also been used. Metvixia® is indicated for the treatment of nonhyperkeratotic AKs of the face and scalp in immunocompetent patients when used with lesion preparation (débridement using a sharp dermal curette) in the physician’s office when other therapies are unacceptable or considered medically less appropriate.

FDA product codes: GEX and LNK.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


