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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.

Populations	Interventions	Comparators	Outcomes
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	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	Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With nonmetastatic invasive squamous cell carcinoma	Interventions of interest are: • Photodynamic therapy	Comparators of interest are: • Cryotherapy • Surgery • Radiotherapy	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With acne	Interventions of interest are: • Photodynamic therapy	Comparators of interest are: • Pharmacologic therapy • Laser or light therapy	Relevant outcomes include: • Symptoms • Change in disease status • Quality of life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With noncancerous dermatologic skin conditions (e.g., hidradenitis suppurativa, mycoses, port wine stain) 	Interventions of interest are: <ul style="list-style-type: none"> • Photodynamic therapy 	Comparators of interest are: <ul style="list-style-type: none"> • Pharmacologic therapy • Cryotherapy • Laser therapy 	Relevant outcomes include: <ul style="list-style-type: none"> • Symptoms • Change in disease status • Quality of life • Treatment-related morbidity

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 non-hyperkeratotic AKs on the face or scalp who receive PDT, the evidence includes 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 in patients with non-hyperkeratotic AKs on the face or scalp compared with placebo or other active interventions. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have non-hyperkeratotic AKs on the upper extremities who receive PDT, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, QOL, and treatment-related morbidity. In two 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 four 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 six months of follow-up. The evidence is sufficient to determine that the technology results in a meaningful 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 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. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have squamous cell carcinoma in situ who receive PDT, the evidence includes RCTs. 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. The evidence is sufficient to determine that the technology results in a meaningful 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. 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 the effects of the technology on health outcomes.

For individuals who have acne who receive PDT, the evidence includes RCTs and a systematic review. 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 a meta-analysis did not find significantly better results with PDT vs. 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 the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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

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 (5-ALA) and its methyl ester, methyl aminolevulinate. When applied topically, these agents pass readily through abnormal keratin overlying the lesion and accumulate preferentially in dysplastic cells. The agents 5-ALA and methyl aminolevulinate 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 non-hyperkeratotic AKs of the face and scalp. In 2018, the indication was expanded to include non-hyperkeratotic 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 5-ALA patch technology is available outside of the US through an agreement between Intendis (now Bayer HealthCare) and Photonamic. The 5-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 aminolevulinate (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 non-hyperkeratotic 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.

RELATED PROTOCOLS

Light Therapy for Psoriasis

Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

Photodynamic Therapy for Choroidal Neovascularization

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.

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