FEP 2.01.44 Dermatologic Applications of Photodynamic Therapy

Effective Date: April 15, 2017

Related Policies
2.01.47 Light Therapy for Psoriasis

5.90.21 Aminolevulinic Acid

8.01.06 Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

9.03.08 Photodynamic Therapy for Choroidal Neovascularization

Dermatologic Applications of Photodynamic Therapy

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, administered orally or intravenously, have been used in nondermatologic applications and are being proposed for use with dermatologic conditions such as actinic keratoses and nonmelanoma skin cancers.

FDA REGULATORY STATUS

In 1999, Levulan® Kerastick™, a topical preparation of aminolevulinic acid (ALA), in conjunction with illumination with the BLU-U™ Blue Light Photodynamic Therapy Illuminator, was approval by the U.S. Food and Drug Administration (FDA) for the following indication: “The Levulan Kerastick for topical solution plus blue light illumination using the BLU-U Blue Light Photodynamic Therapy Illuminator is indicated for the treatment of nonhyperkeratotic actinic keratoses of the face and scalp.” The product is applied in the physician’s office. FDA product code: MVF.

A 5-aminolevulinic acid patch technology (5-ALA patch) is available outside of the United States through an agreement between Intendis (part of Bayer HealthCare) and Photonamic. The 5-ALA patch is not approved by FDA.

Another variant of photodynamic therapy for skin lesions is Metvixia® used with the Aktilite CL128 lamp, each of which received FDA approval in 2004. Metvixia® (Galderma, Switzerland; Photocure, Norway) 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 nonhyperkeratotic actinic keratoses 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.

POLICY STATEMENT

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

- Nonhyperkeratotic actinic keratoses of the face and scalp.
- Low-risk (eg, superficial and nodular) basal cell skin cancer only when surgery and radiation are contraindicated.
- Bowen disease (squamous cell carcinoma in situ) 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 is considered **not medically necessary**.

POLICY GUIDELINES

Surgery and radiation are the preferred treatments for low-risk basal cell cancer and Bowen disease (see Rationale section). 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 compared with surgery or radiation.

Photodynamic therapy typically involves 2 office visits: one to apply the topical aminolevulinic acid and a second visit to expose the patient to blue light. The second physician office visit, performed solely to administer blue light, should not warrant a separate Evaluation and Management CPT code. Photodynamic protocols typically involve 2 treatments spaced a week apart; more than 1 treatment series may be required.

RATIONALE

Summary of Evidence

For individuals who have nonhyperkeratotic actinic keratoses on the face or scalp who receive photodynamic therapy (PDT), the evidence includes randomized controlled trials (RCTs). Relevant outcomes are symptoms, change in disease status, quality of life, and treatment-related morbidity. Evidence from multiple RCTs has found that PDT improves the net health outcome in patients with nonhyperkeratotic actinic keratoses 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 low-risk basal cell carcinoma (BCC) who receive PDT, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are symptoms, change in disease status, quality of life, and treatment-related morbidity. Systematic reviews of RCTs have found that PDT may not be as effective as surgery for superficial and nodular BCC. In the small number of trials available, PDT was more effective than 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, quality of life, and treatment-related morbidity. RCTs have found that PDT has similar or greater efficacy compared with cryotherapy and 5-fluorouracil. Additionally, adverse events/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, quality of life, 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, quality of life, and treatment-related morbidity. The available RCTs have not consistently found significantly better outcomes with PDT compared with comparison interventions and a meta-analysis did not find significantly better results with PDT versus placebo. Several trials have found that PTD is associated with high rates of adverse events leading to 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 skin conditions (eg, hidradenitis suppurativa, mycoses, or port wine stain) who receive PDT, the evidence case series and systematic reviews of uncontrolled series. Relevant outcomes are symptoms, change in disease status, quality of life, 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Canadian Dermatology Association

In 2015, the Canadian Dermatology Association published the following recommendations on dermatologic use of photodynamic therapy (PDT):

- Basal cell carcinoma (BCC): PDT may be used for superficial BCC when nonsurgical treatment is desired, there are multiple carcinomas, and when cosmetic outcome is important. PDT is not appropriate for nodular BCC.[33]

- Actinic keratosis: PDT is among the recommended treatment options for actinic keratosis, although the guidance includes the statement that cryosurgery or a surgical procedure are preferred for isolated actinic keratosis and hypertonic lesions.[34]

National Comprehensive Cancer Network

National Comprehensive Cancer Network (NCCN) guidelines on basal cell skin cancers (v.1.2017) state: “Since cure rates may be lower, superficial therapies should be reserved for those patients where surgery or radiation is contraindicated or impractical. Superficial therapies include topical treatment with 5-FU [5-fluorouracil] or imiquimod, photodynamic therapy (PDT) and cryotherapy.” In addition, NCCN concluded that, although the cure rate may be lower, for patients with low-risk superficial BCC where surgery or

radiation is contraindicated or impractical, first-line treatment with alternative therapies such as PDT, cryotherapy, 5-FU, or imiquimod may be considered.[35]

British Association of Dermatologists

In 2008, the British Association of Dermatologists published guidelines stating the following on PDT:

"Multicentre randomized controlled studies now demonstrate high efficacy of topical photodynamic therapy (PDT) for actinic keratoses, Bowen's disease (BD) and superficial basal cell carcinoma (BCC), and efficacy in thin nodular BCC, while confirming the superiority of cosmetic outcome over standard therapies. Long-term follow-up studies are also now available, indicating that PDT has recurrence rates equivalent to other standard therapies in BD and superficial BCC, but with lower sustained efficacy than surgery in nodular BCC. In contrast, current evidence does not support the use of topical PDT for squamous cell carcinoma.... There is an accumulating evidence base for the use of PDT in acne, while detailed study of an optimized protocol is still required."[36]

International Society for Photodynamic Therapy in Dermatology

The International Society for Photodynamic Therapy in Dermatology (ISPTD) published consensus-based guidelines on the use of PDT for nonmelanoma skin cancer in 2005. Based on both efficacy and cosmetic outcome, ISPTD recommended PDT as a first-line therapy for actinic keratosis. ISPTD considered aminolevulinic acid not to have sufficient tissue penetration for nodular BCC. Based on 2 randomized controlled and 3 open-label studies, it was concluded that methyl aminolevulinate PDT could be effective for nodular BCC lesions less than 2 mm in depth, if debulked. The guidelines recommended PDT for superficial BCC as "a viable alternative when surgery would be inappropriate or the patient or physician wishes to maintain normal skin appearance." The guidelines also concluded that PDT is at least as effective as cryotherapy or 5-fluorouracil for Bowen disease but that there is insufficient evidence to support the routine use of topical PDT for squamous cell carcinoma.[37]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

Centers for Medicare and Medicaid Services coverage policy on treatment of actinic keratosis dated November 26, 2001, noted:

> "Various options exist on treating AKs [actinic keratosis]. Clinicians should select an appropriate treatment based on the patient's history, the lesion's characteristics, and the patient's preference for specific treatment…. Less commonly performed treatments for AK include dermabrasion, excision, chemical peels, laser therapy, and photodynamic therapy....
>
> Medicare covers the destruction of actinic keratosis without restrictions based on lesion or patient characteristics."[38]

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POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
March 2013	Update Policy	Policy updated with literature review; References added, renumbered or removed. Policy statements unchanged.
March 2014	Update Policy	Literature updated with references 6, 13, 17, 20, and 23 added, other references removed or reorganized. Policy statements unchanged.
March 2015	Update Policy	Policy updated with literature review through December 15, 2014; references 3, 7-10 and 12 added and reference 30 updated. In medically necessary statement, superficial basal cell carcinoma changed to low-risk (ie superficial or nodular) basal cell carcinoma. In investigational statement, non- superficial basal cell carcinoma changed to high-risk basal cell carcinoma.
June 2016	Update Policy	Policy updated with literature review through December 6, 2015; references 29-30 and 32-33 added. Policy statements unchanged.
March 2017	Update Policy	Policy updated with literature review through October 26, 2016; references 13, 17, and 22-23 added. Policy statements unchanged.