Dermatologic Applications of Photodynamic Therapy

**Description of Procedure or Service**

Photodynamic therapy (PDT) refers to light activation of a photosensitizer to generate highly reactive oxygen intermediaries, which ultimately cause tissue injury and necrosis. Photosensitizing agents, administered orally or intravenously, have been used in non-dermatologic applications and are being proposed for use with dermatologic conditions such as actinic keratoses and non-melanoma skin cancers.

Two common photosensitizing agents are 5-aminolevulinic acid (5-ALA) and its methyl ester methyl aminolevulinate (MAL). When applied topically, they pass readily through the abnormal keratin overlying the lesion and accumulates preferentially in dysplastic cells. 5-ALA and MAL are metabolized by the underlying cells to photosensitizing concentrations of porphyrins. Subsequent exposure to photoactivation (maximum absorption at 404–420 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. It has also been investigated as a treatment of other superficial dermatologic lesions, such as Bowen’s disease, acne vulgaris, mycoses, hidradenitis suppurativa, and superficial and nodular basal cell carcinoma. Potential cosmetic indications include skin rejuvenation and hair removal.

Actinic keratoses are rough, scaly, or warty premalignant growths on sun-exposed skin that are very common in older individuals with fair complexions, with a prevalence of >80% in fair-skinned people over the age of 60. In some cases actinic keratosis may progress to squamous cell carcinoma. The available treatments for actinic keratoses can generally be divided into surgical and non-surgical methods. Surgical treatments used to treat one or a small number of dispersed individual lesions include excision, curettage (either alone or combined with electrodisccation), and laser surgery. Non-surgical treatments include cryotherapy, topical chemotheraphy (5-fluorouracil [5-FU] or masoprocol creams), chemexfoliation (also known as chemical peels), and dermabrasion. Topical treatments are generally used in patients with multiple lesions and the involvement of extensive areas of skin. Under some circumstances, combinations of different treatment methods may be used.

Non-melanoma skin cancers are the most common malignancies in the Caucasian population. Basal cell carcinoma (BCC) is most often found in light-skinned individuals and is the most common of the cutaneous malignancies. Although the tumors rarely metastasize, they can be locally invasive if left untreated, leading to significant local destruction and disfigurement. The most prevalent forms of BCC are nodular BCC and superficial BCC. Bowen’s disease is a squamous cell carcinoma (SCC) in situ with the potential for significant lateral spread. Metastases are rare, with less than 5% of cases advancing to invasive SCC. Lesions may appear on sun-exposed or covered skin. Excision surgery is the preferred treatment for smaller non-melanoma skin lesions and those not in problematic areas, such as the face and digits. Other established treatments include topical 5-fluorouracil, imiquimod, and cryotherapy. Poor cosmesis resulting from surgical procedures and skin irritation induced by topical agents can be significant problems.
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Regulatory Status

In 1999, Levulan® Kerastick™, a topical preparation of ALA, in conjunction with illumination with the BLUU™ Blue Light Photodynamic Therapy Illuminator, received 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 non-hyperkeratotic actinic keratoses of the face and scalp.” The product is applied in the physician’s office.

A 5-aminolevulinic acid patch technology (5-ALA Patch) is available outside of the U.S through an agreement between Intendis (part of Bayer HealthCare) and Photonamic GmbH and Co. KG. The 5-ALA patch is not approved by the FDA.

Another variant of PDT for skin lesions is Metvixia® and the Aktilite CL128 lamp, each of which received FDA approval in July 2004. Metvixia® (Galderma, SA, Switzerland; PhotoCure ASA, Norway) consists of the topical application of methyl aminolevulinate (MAL) in contrast to ALA used in the Kerastick procedure, followed by exposure with the Aktilite CL 128 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 (IPL), pulsed dye lasers (PDL), and potassium titanyl phosphate (KTP) lasers have also been used. Metvixia is indicated for the treatment of non-hyperkeratotic actinic keratoses of the face and scalp in immunocompetent patients when used in conjunction with lesion preparation (debridement using a sharp dermal curette) in the physician's office when other therapies are unacceptable or considered medically less appropriate.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for dermatologic applications of photodynamic therapy when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Dermatologic Applications of Photodynamic Therapy is covered

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

- Non-hyperkeratotic actinic keratoses of the face and scalp.
- Low-risk (e.g. superficial and nodular) basal cell skin cancer only when surgery and radiation are contraindicated.
- Bowen’s disease (squamous cell carcinoma in situ) only when surgery and radiation are contraindicated.
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When Dermatologic Applications of Photodynamic Therapy is not covered

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.

Photodynamic therapy is considered not medically necessary as a treatment of non-hyperkeratotic actinic keratoses in locations other than the face and scalp, including, but not limited to, the trunk and extremities.

Policy Guidelines

Photodynamic therapy refers to light activation of a photosensitizing agent light to produce photochemical effects in the target area. The evidence to date suggests that the net health outcome is better with surgery than with PDT for treating BCC and that PDT for superficial BCC has a similar efficacy to cryotherapy and better cosmetic outcomes. In addition, there is evidence from RCTs that PDT is an effective treatment for selected patients with actinic keratoses of the face and scalp compared to placebo or cryotherapy. There is insufficient evidence that PDT improves the net health outcome for nodular BCC and other dermatological conditions compared to accepted treatments. Thus, PDT may be considered medically necessary for treating selected patients with actinic keratoses, superficial BCC, and Bowen’s disease and is considered investigational for all other dermatologic indications.

There is evidence from randomized controlled trials (RCTs) that photodynamic therapy (PDT) is an effective treatment for selected patients with actinic keratoses of the face and scalp compared with placebo or cryotherapy. The evidence to date suggests that PDT is less effective than surgery and radiotherapy and of similar efficacy to cryotherapy for treating low-risk basal cell carcinoma (BCC) (eg, superficial and nodular). Moreover, the evidence suggests that cosmetic outcomes are better after PDT compared with surgery and cryotherapy. Evidence from randomized controlled trials RCTs suggests that, in patients with Bowen disease (BD), PDT has similar or higher efficacy compared with cryotherapy and 5-fluorouracil, and better cosmetic outcomes. Thus, PDT may be considered medically necessary for treating non-hyperkeratotic actinic keratoses of the face and scalp, and for treating low-risk BCC and BD when surgery and radiation are contraindicated.

The v 1.2015 clinical practice guideline on basal cell skin cancers from the National Comprehensive Cancer Network (NCCN) states: “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 or imiquimod, photodynamic therapy (PDT) and cryotherapy.” Moreover, the guideline describes BCC histologic subtypes that have low-risk recurrence as nodular, superficial, and other non-aggressive growth patterns, such as keratotic, infundibulocystic, and fibroepithelioma of Pinkus. For patients with low-risk BCCs the guidelines states,”... topical therapies such as 5-FU (5-fluorouracil), imiquimod, PDT (eg, porfimer sodium or topical amino levulinic acid) or vigorous cryotherapy may be considered even though the cure rate may be lower.”

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina website at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.
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Applicable service codes: 96567, J7308, J7309

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

For EBG entitled: Photodynamic Therapy for the Treatment of Actinic Keratoses

BCBSA Medical Policy Reference Manual, 2.01.44; 11/20/01


BCBSA Medical Policy Reference Manual; 2.01.44; 4/29/03


For policy re-titled: Dermatologic Applications of Photodynamic Therapy


Specialty Matched Consultant Advisory panel review 1-2011

Dermatologic Applications of Photodynamic Therapy


Medical Director review 1/2012

Specialty Matched Consultant Advisory Panel review 1/2012

Medical Director review 5/2012


Specialty Matched Consultant Advisory Panel review 1/2013


Specialty Matched Consultant Advisory Panel review 1/2014

Medical Director review 1/2014

Specialty Matched Consultant Advisory Panel review 1/2015

Medical Director review 2/2015

Policy Implementation/Update Information

For EBG entitled: Photodynamic Therapy for the Treatment of Actinic Keratoses


10/20/05 Description section expanded to include discussion of Metvix therapy. Under "When Covered" section added the following: "Photodynamic therapy with methyl aminolevulinate and exposure to red light may be considered medically necessary as a treatment of non-hyperkeratotic actinic keratoses of the face and scalp only." Under "When not Covered" section, added the following: "Photodynamic therapy with methyl aminolevulinate and exposure to red light is considered investigational for the treatment of other dermatologic applications, including but not limited to basal cell carcinomas, Bowen’s disease, acne vulgaris, mycoses, or squamous cell carcinoma. Photodynamic therapy as a technique of skin rejuvenation, hair removal, or other cosmetic indications is considered not medically necessary." Added acne vulgaris, mycoses and hidradenitis suppurativa as investigational indications for ALA. Notification given 10/20/05. Effective date 1/5/06.

8/21/06 Medical Policy changed to Evidence Based Guideline. (pmo)
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5/21/07 Reference sources added. No changes to criteria. (pmo)

For policy re-titled: Dermatologic Applications of Photodynamic Therapy

6/22/09 EBG name changed from "Photodynamic Therapy for the Treatment of Actinic Keratoses" to "Dermatologic Applications of Photodynamic Therapy". Description section revised. Evidence Based Guideline section now reads "Photodynamic therapy may be appropriate as a treatment of: Non-hyperkeratotic actinic keratoses of the face and scalp; Superficial basal cell skin cancer only when surgery and radiation are contraindicated; Bowen’s disease (squamous cell carcinoma in situ) only when surgery and radiation are contraindicated."

Under When Not Recommended section-first paragraph now reads: "Photodynamic therapy is not recommended for other dermatologic applications, including, but not limited to, acne vulgaris, non-superficial basal cell carcinomas, hidradenitis suppurativa, or mycoses."
Second paragraph has been deleted. Medical term definitions and reference sources added. (pmo)

6/22/10 Policy Guideline Number(s) removed (amw)


2/7/12 Specialty Matched Consultant Advisory Panel review 1/2012. References updated. Description section updated. Medical Director review 1/2012. No changes to Policy Statements. (mco)

6/12/12 Evidence Based Guideline converted to Corporate Medical Policy. Photodynamic therapy may be considered medically necessary as a treatment of: Non-hyperkeratotic actinic keratoses of the face and scalp, Superficial basal cell skin cancer only when surgery and radiation are contraindicated, Bowen’s 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, non-superficial basal cell carcinomas, hidradenitis suppurativa, or mycoses. Photodynamic therapy as a technique of skin rejuvenation, hair removal, or other cosmetic indications is considered not medically necessary. Photodynamic therapy is considered not medically necessary as a treatment of non-hyperkeratotic actinic keratoses in locations other than the face and scalp, including, but not limited to, the trunk and extremities. Medical Director review 5/2012. Notice given 6/12/12 for effective date 9/18/12. (mco)


2/24/15 Specialty Matched Consultant Advisory Panel review 1/2015. Medical Director review 2/2015. When Covered section updated to add, “Low-risk (e.g. superficial and nodular)” to the second bullet. When Not Covered section updated to remove “superficial” and add “high risk”. Policy Guidelines section updated. References updated. (td)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.