

Evidence Based Guideline

Dermatologic Applications of Photodynamic Therapy

File Name: dermatologic_applications_of_photodynamic_therapy
Guideline Number: EBG.MED1335
Origination: 10/2003
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Last Review: 5/2009

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**.

When applied topically, the **photosensitizing agent** 5-aminolevulinic acid (5-ALA) or its methyl ester methyl aminolevulinate (MAL) passes 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 **electrodesiccation**), and laser surgery. Non-surgical treatments include **cryotherapy**, topical chemotherapy (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.

In 1999, Levulan® Kerastick™, a topical preparation of ALA, in conjunction with illumination with the BLU-U™ 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

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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.”

As described in the package insert, the technique involves 2 steps starting with application of the ALA Topical Solution in the physician's office. The package insert recommends that the application should involve either face or scalp lesions, but not both simultaneously. The patient is told to return in 14 to 18 hours, at which point the lesion is exposed to blue light for 17 minutes. During this period, the patient experiences sensations of tingling, stinging, or burning of the treated lesions. Treated lesions, that have not completely resolved after 8 weeks, may be treated a second time.

Another variant of PDT for skin lesions is Metvixia® and the CureLight BroadBand (Model CureLight 01), 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 CureLight BroadBand, a proprietary 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.

PhotoCure also sought FDA approval of Metvixia for the treatment of basal cell carcinomas. However, the indication for basal cell carcinomas was not approved by the FDA. Levulan is marketed in the United States while Metvixia is marketed in Europe.

Evidence Based Guideline for the Dermatologic Applications of Photodynamic Therapy

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.

Medical Evidence regarding the Dermatologic Applications of Photodynamic Therapy indicates it is not recommended in the following situations:

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.

Photodynamic therapy as a technique of skin rejuvenation, hair removal, or other cosmetic indications is considered not medically necessary.

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the policy.

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 web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 96567, J7308

Medical Term Definitions

Cosmesis

preservation, restoration, or enhancement of physical appearance

Cryotherapy

the therapeutic use of cold; especially cryosurgery.

Curettage

a surgical scraping or cleaning by means of a curette.

Cytotoxic

toxic to cells.

Electrodesiccation

the drying of tissue by a high-frequency electric current applied with a needle-shaped electrode—called also fulguration.

Erythema

redness of the skin produced by congestion of the capillaries.

Immunocompetent

able to develop an immune response. Able to recognize antigens and respond to them. The opposite of immunodeficient.

In situ

in the natural or original position or place; an in situ cancer confined to the breast duct.

Metastases

transmission of pathogenic microorganisms or cancerous cells from an original site to one or more sites elsewhere in the body, usually by way of the blood vessels or lymphatics; all malignant tumors are capable of metastasizing.

Necrosis

death of cells or groups of cells.

Photosensitizing agent

drugs that when exposed to ultraviolet radiation or sunlight have a beneficial effect on diseased tissue. They can be administered on the skin or taken internally. They can be used to treat skin conditions and types of tumors.

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

ECRI TARGET Report # 810. Photodynamic therapy (PDT) with aminolevulinic acid for treatment of actinic keratosis (AK). November, 2001.

ECRI Hotline Response: Photodynamic Therapy (PDT) with Aminolevulinic Acid for Treatment of Actinic Keratosis (AK). January 27, 2003.

Coverage Issues Manual Section 35-101. Treatment of Actinic Keratosis. Accessed 1/22/2003. http://www.cms.hhs.gov/manuals/06_cim/ci35.asp#sect_35_101

Specialty Matched Consultant Advisory Panel - 3/2003

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

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.44, 4/16/04.

Specialty Matched Consultant Advisory Panel - 2/11/2005

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.44, 4/1/05.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.44, 7/20/06.

For EBG renamed: Dermatologic Applications of Photodynamic Therapy

Specialty Matched Consultant Advisory Panel - 4/27/07.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.44, 8/2/07.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.44, 8/14/08.

Specialty Matched Consultant Advisory Panel - 5/2009.

Policy Implementation/Update Information

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

10/03 Specialty Matched Consultant Advisory Panel review 3/03. Original Policy issued.

3/3/05 Specialty Matched Consultant Advisory Panel review 2/2005. No changes to criteria. References added.

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)

5/21/07 Reference sources added. No changes to criteria. (pmo)

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For EBG renamed: 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)

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