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OVERVIEW

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.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Commercial Products

Photodynamic therapy is medically necessary as a treatment of nonhyperkeratotic actinic keratoses of the face and scalp, nonhyperkeratotic actinic keratoses of the upper extremities, superficial basal cell skin cancer only when surgery and radiation are contraindicated, and for the treatment of Bowen disease (squamous cell carcinoma in situ) only when surgery and radiation are contraindicated.

Photodynamic therapy is not medically necessary for all other dermatologic applications, including, but not limited to, acne vulgaris, high-risk basal cell carcinoma, hidradenitis suppurativa, and mycoses, or as a technique of skin rejuvenation, hair removal, or other cosmetic indications as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable medical and not medically necessary benefits/coverage.

BACKGROUND

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 and nonmelanoma skin cancers.

For individuals who have nonhyperkeratotic actinic keratoses on the face or scalp who receive PDT, the evidence includes randomized controlled trials (RCTs). The 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 nonhyperkeratotic AKs on the upper extremities who receive PDT, the evidence includes RCTs. The 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 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 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. The 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 basal cell carcinoma. 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. The 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 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. The 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. The 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 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 (eg, 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. The 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.

CODING

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The following codes are considered medically necessary when filed with the one of the diagnosis below:

96567 Photodynamic therapy by external application of light to destroy premalignant and/or malignant lesions of the skin and adjacent mucosa (e.g., lip) by activation of photosensitive drug(s), each phototherapy exposure session.

96573 Photodynamic therapy by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day

96574 Debridement of premalignant hyperkeratotic lesion(s) (ie, targeted curettage, abrasion) followed with photodynamic therapy by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day

J7308 Aminolevulinic hydrochloric acid for topical administration, 20%, single unit dosage form (354 mg)

J7309 Methyl aminolevulinate (MAL) for topical administration, 16.8%, 1 gram

ICD10 codes:

B36.8-B36.9

B48.8-B49

C44.0-C44.9

D04.0-D04.9

L57.0

L70.0

L73.2

Q82.5

RELATED POLICIES

BlueCHiP for Medicare National and Local Coverage Determinations

PUBLISHED

Provider Update, May 2020

Provider Update, June 2019

Provider Update, February 2019

Provider Update, March 2017

Provider Update, May 2016

REFERENCES

1. Pariser DM, Lowe NJ, Stewart DM, et al. Photodynamic therapy with topical methyl aminolevulinate for actinic keratosis: results of a prospective randomized multicenter trial. *J Am Acad Dermatol*. Feb 2003;48(2):227-232. PMID 12582393

2. Morton C, Campbell S, Gupta G, et al. Intraindividual, right-left comparison of topical methyl aminolaevulinate-photodynamic therapy and cryotherapy in subjects with actinic keratoses: a multicentre, randomized controlled study. *Br J Dermatol*. Nov 2006;155(5):1029-1036. PMID 17034536

3. Hauschild A, Stockfleth E, Popp G, et al. Optimization of photodynamic therapy with a novel self-adhesive 5-aminolaevulinic acid patch: results of two randomized controlled phase III studies. *Br J Dermatol*. May 2009;160(5):1066-1074. PMID 19222455

4. Szeimies RM, Radny P, Sebastian M, et al. Photodynamic therapy with BF-200 ALA for the treatment of actinic keratosis: results of a prospective, randomized, double-blind, placebo-controlled phase III study. *Br J Dermatol*. Aug 2010;163(2):386-394. PMID 20518784

5. Szeimies RM, Stockfleth E, Popp G, et al. Long-term follow-up of photodynamic therapy with a self-adhesive 5-aminolaevulinic acid patch: 12 months data. *Br J Dermatol*. Feb 1 2010;162(2):410-414. PMID 19804593

6. Serra-Guillen C, Nagore E, Hueso L, et al. A randomized pilot comparative study of topical methyl aminolevulinate photodynamic therapy versus imiquimod 5% versus sequential application of both therapies in immunocompetent patients with actinic keratosis: clinical and histologic outcomes. *J Am Acad Dermatol*. Apr 2012;66(4):e131-137. PMID 22226430

7. Dirschka T, Radny P, Dominicus R, et al. Photodynamic therapy with BF-200 ALA for the treatment of actinic keratosis: results of a multicentre, randomized, observer-blind phase III study in comparison with a registered methyl-5-aminolaevulinate cream and placebo. *Br J Dermatol*. Jan 2012;166(1):137-146. PMID 21910711
8. Dirschka T, Radny P, Dominicus R, et al. Long-term (6 and 12 months) follow-up of two prospective, randomized, controlled phase III trials of photodynamic therapy with BF-200 ALA and methyl aminolaevulinate for the treatment of actinic keratosis. *Br J Dermatol*. Apr 2013;168(4):825-836. PMID 23252768
9. Giehl KA, Kriz M, Grahovac M, et al. A controlled trial of photodynamic therapy of actinic keratosis comparing different red light sources. *Eur J Dermatol*. May-Jun 2014;24(3):335-341. PMID 24876164
10. Rubel DM, Spelman L, Murrell DF, et al. Daylight photodynamic therapy with methyl aminolevulinate cream as a convenient, similarly effective, nearly painless alternative to conventional photodynamic therapy in actinic keratosis treatment: a randomized controlled trial. *Br J Dermatol*. Nov 2014;171(5):1164-1171. PMID 24861492
11. Neittaanmaki-Perttu N, Karppinen TT, Gronroos M, et al. Daylight photodynamic therapy for actinic keratoses: a randomized double-blinded nonsponsored prospective study comparing 5-aminolaevulinic acid nanoemulsion (BF-200) with methyl-5-aminolaevulinate. *Br J Dermatol*. Nov 2014;171(5):1172-1180. PMID 25109244
12. Zane C, Facchinetti E, Rossi MT, et al. A randomized clinical trial of photodynamic therapy with methyl aminolaevulinate vs. diclofenac 3% plus hyaluronic acid gel for the treatment of multiple actinic keratoses of the face and scalp. *Br J Dermatol*. May 2014;170(5):1143-1150. PMID 24506666
13. Reinhold U, Dirschka T, Ostendorf R, et al. A randomized, double-blind, phase III, multicentre study to evaluate the safety and efficacy of BF-200 ALA (Ameluz((R))) vs. placebo in the field-directed treatment of mild-to-moderate actinic keratosis with photodynamic therapy (PDT) when using the BF-RhodoLED((R)) lamp. *Br J Dermatol*. Oct 2016;175(4):696-705. PMID 26921093
14. Yazdanyar S, Zarchi K, Jemec GBE. Pain during topical photodynamic therapy - comparing methyl aminolevulinate (Metvix((R))) to aminolaevulinic acid (Ameluz((R))); an intra-individual clinical study. *Photodiagnosis Photodyn Ther*. Aug 02 2017. PMID 28780136
15. Patel G, Armstrong AW, Eisen DB. Efficacy of photodynamic therapy vs other interventions in randomized clinical trials for the treatment of actinic keratoses: a systematic review and meta-analysis. *JAMA Dermatol*. Dec 2014;150(12):1281-1288. PMID 25162181
16. Wang H, Xu Y, Shi J, et al. Photodynamic therapy in the treatment of basal cell carcinoma: a systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed*. Jan 2015;31(1):44-53. PMID 25377432
17. Zou Y, Zhao Y, Yu J, et al. Photodynamic therapy versus surgical excision to basal cell carcinoma: meta-analysis. *J Cosmet Dermatol*. Dec 2016;15(4):374-382. PMID 27363535
18. Bath-Hextall FJ, Perkins W, Bong J, et al. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev*. Jan 24 2007(1):CD003412. PMID 17253489
19. Roozeboom MH, Arits AH, Mosterd K, et al. Three-year follow-up results of photodynamic therapy vs. imiquimod vs. fluorouracil for treatment of superficial basal cell carcinoma: a single-blind, noninferiority, randomized controlled trial. *J Invest Dermatol*. Aug 2016;136(8):1568-1574. PMID 27113429

20. Szeimies RM, Ibbotson S, Murrell DF, et al. A clinical study comparing methyl aminolevulinate photodynamic therapy and surgery in small superficial basal cell carcinoma (8-20 mm), with a 12-month follow-up. *J Eur Acad Dermatol Venereol*. Nov 2008;22(11):1302-1311. PMID 18624836
21. Rhodes LE, de Rie M, Enstrom Y, et al. Photodynamic therapy using topical methyl aminolevulinate vs surgery for nodular basal cell carcinoma: results of a multicenter randomized prospective trial. *Arch Dermatol*. Jan 2004;140(1):17-23. PMID 14732655
22. Rhodes LE, de Rie MA, Leifsdottir R, et al. Five-year follow-up of a randomized, prospective trial of topical methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma. *Arch Dermatol*. Sep 2007;143(9):1131-1136. PMID 17875873
23. Bath-Hextall FJ, Matin RN, Wilkinson D, et al. Interventions for cutaneous Bowen's disease. *Cochrane Database Syst Rev*. Jun 24 2013;6(6):CD007281. PMID 23794286
24. Morton C, Horn M, Leman J, et al. Comparison of topical methyl aminolevulinate photodynamic therapy with cryotherapy or Fluorouracil for treatment of squamous cell carcinoma in situ: Results of a multicenter randomized trial. *Arch Dermatol*. Jun 2006;142(6):729-735. PMID 16785375
25. Salim A, Leman JA, McColl JH, et al. Randomized comparison of photodynamic therapy with topical 5-fluorouracil in Bowen's disease. *Br J Dermatol*. Mar 2003;148(3):539-543. PMID 12653747

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