



Health Net

National Medical Policy

Subject: Acne Treatments

Policy Number: NMP360

Effective Date*: August 2007

Updated: August 2015

**This National Medical Policy is subject to the terms in the
IMPORTANT NOTICE
at the end of this document**

For Medicaid Plans: Please refer to the appropriate Medicaid Manuals for coverage guidelines prior to applying Health Net Medical Policies

The Centers for Medicare & Medicaid Services (CMS)

For Medicare Advantage members please refer to the following for coverage guidelines first:

Use	Source	Reference/Website Link
	National Coverage Determination (NCD)	
	National Coverage Manual Citation	
X	Local Coverage Determination (LCD)*	Plastic Surgery: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx
	Article (Local)*	
	Other	
	None	Use Health Net Policy

Instructions

- Medicare NCDs and National Coverage Manuals apply to ALL Medicare members in ALL regions.
- Medicare LCDs and Articles apply to members in specific regions. To access your specific region, select the link provided under "Reference/Website" and follow the search instructions. Enter the topic and your specific state to find the coverage determinations for your region. ***Note: Health Net must follow local coverage determinations (LCDs) of Medicare Administration Contractors (MACs) located outside their service area when those MACs have exclusive coverage of an item or service. (CMS Manual Chapter 4 Section 90.2)**
- If more than one source is checked, you need to access all sources as, on occasion, an LCD or article contains additional coverage information than contained in the NCD or National Coverage Manual.
- If there is no NCD, National Coverage Manual or region specific LCD/Article, follow the Health Net Hierarchy of Medical Resources for guidance.

Current Policy Statement

Health Net Inc. considers any of the following (alone or in combination) medically necessary for the treatment of active acne vulgaris:

- Topical Therapy (e.g. benzoyl peroxide, topical retinoids, topical antibiotics)
- Systemic antibiotics (e.g. doxycycline, minocycline, tetracycline)
- Hormonal agents in females (e.g. oral contraceptives, spironolactone and cyproterone acetate)
- Oral retinoids (Isotretinoin) for severe recalcitrant nodular acne or treatment resistant acne
- Acne surgery (e.g., comedo removal or incision and drainage) for management of comedones resistant to other therapies
- Intralesional steroids for large inflammatory lesions in conjunction with other treatments

Health Net Inc. considers any of the following for the treatment of active acne investigational due to inadequate scientific evidence in the medical literature validating their effectiveness:

- Phototherapy
- Photodynamic therapy (with and without pretreatment with topical medications)
- Laser therapy
- Dermabrasion and microdermabrasion
- Cryotherapy/cryoslush therapy (solid CO2 mixed with acetone) and liquid nitrogen therapy
- Chemical peels

Health Net Inc. considers any of the following for the treatment of acne scarring cosmetic:

- Chemical Peels
- Dermabrasion
- Dermal or epidermal chemical peels
- Dermal fillers
- Laser resurfacing (e.g. CO2, Yag laser, KTP laser)
- Microdermabrasion
- Phototherapy
- Photodynamic therapy
- Punch excision
- Punch elevation
- Subcutaneous incision (Subcision)
- Scar excision

Codes Related To This Policy

NOTE:

The codes listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the benefit documents and medical necessity criteria. This list of codes may not be all inclusive.

On October 1, 2015, the ICD-9 code sets used to report medical diagnoses and inpatient procedures will be replaced by ICD-10 code sets. Health Net National Medical Policies will now include the preliminary ICD-10 codes in preparation for this transition. Please note that these may not be the final versions of the codes and

that will not be accepted for billing or payment purposes until the October 1, 2015 implementation date.

ICD-9 Codes

706.1 Other acne

ICD-10 Codes

L70.0 Acne vulgaris
L70.1 Acne conglobata
L70.8 Other Acne

CPT Codes

10040 Acne Surgery (e.g., marsupialization, opening or removal of multiple milia, comedones, cysts pustules)
11900 Injection, Intralesional; up to and including seven lesions
11901 Injection, Intralesional; more than seven lesions
17340 Cryotherapy (CO2 slush, liquid N2) for acne
17360 Chemical exfoliation for acne (eg, acne paste, acid)
96999 Unlisted special dermatological service or procedure

HCPCS Codes

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

Scientific Rationale – Update August 2015

Moneib et al (2014) reported the 1,550-nm erbium glass laser is one of the infrared lasers that may be useful in the treatment of acne. The authors sought to evaluate the efficacy of an erbium glass laser in treatment of active acne and to study the effect of this type of laser on sebaceous glands. Twenty-four patients with active acne lesions were treated using 1,550-nm (30-40 mJ) fractional erbium glass laser. Every patient received 4 sessions with a 2-week interval. Follow-up was done every 3 months for 1 year. The image analyzer computer system was used to measure the sebaceous gland size. A significant reduction ($p < .0001$) in the mean count of lesions was observed after treatment and in the follow-up period. A significant reduction in the size of sebaceous glands was also evident after laser treatment. The authors concluded treatment of active acne with the 1,550-nm erbium glass laser is effective. Papules, pustules, and nodules all respond well to therapy. The sebaceous gland size decreased significantly, which accounts for the long remission period.

Dong et al (2015) investigated the efficacy and safety of a newly designed LED device used in photodiagnosis and photodynamic therapy of moderate to severe acne vulgaris in Chinese patients. Forty-six patients with moderate to severe facial acne showing high degrees of fluorescence by ultraviolet light examination were illuminated during aminolevulinic acid (ALA)- photodynamic therapy (PDT) with two wavelengths of light (543-548nm, and 630 ± 6 nm, respectively) after 2h of incubation with ALA. Each patient received treatment once every 30 days for two or three sessions. Two independent investigators assigned an acne severity score at baseline, one week after each treatment, as well as 4, 8, and 12 weeks after the completion of treatment. Adverse effects were recorded during and after each treatment. All patients rated their satisfaction with the results of treatment at a 12-week follow up visit. The ALA-PDL treatment regimen showed an overall effectiveness rate of 89.13% (41/46 patients). Some degree of clinical efficacy was seen in 71.42%, 86.67%, and 95.83% of patients with grades IV, V, and VI acne, respectively, and the rate of clinical effectiveness increased with increasing acne

severity. When compared with baseline scores, significant reductions in acne scores were obtained at 8, and 12 weeks after completion of treatment. Maximum efficacy was shown at the 12 week follow up. No severe adverse events were observed. The authors concluded ALA-PDT administered with the newly designed LED device was an effective treatment for moderate to severe acne vulgaris, and side effects were mild and reversible.

Ma et al (2014) aimed to evaluate the effectiveness and safety of topical 5-aminolevulinic acid (ALA)-mediated photodynamic therapy (PDT) for the treatment of severe acne in Chinese adolescent patients. Twenty-one Chinese adolescent patients aged 12-18 years with Pillsbury III-IV severe facial acne were treated with three courses of ALA-PDT. A 5% ALA lotion was applied topically for 60 min followed by irradiation with light-emitting diode light at 633 nm with a light intensity of 75-80 mW/cm² and a light dose of 90-96 J/cm². Clinical assessment was conducted before and after each treatment, and at each follow-up session. The total effective rates were 85.71%, 90.48%, and 95.23% after the three PDT sessions, and at the 4- and 8-week follow ups, respectively. ALA-PDT is an effective treatment for severe adolescent acne vulgaris, and is associated with mild and reversible side-effects.

Scientific Rationale – Update August 2013

Eichenfield et al (2013) reported that current acknowledged guidelines for the diagnosis and management of pediatric acne are lacking, and there are variations in management across the spectrum of primary and specialty care. The American Acne and Rosacea Society convened a panel of pediatric dermatologists, pediatricians, and dermatologists with expertise in acne to develop recommendations for the management of pediatric acne and evidence-based treatment algorithms. Ten major topic areas in the diagnosis and treatment of pediatric acne were identified. A thorough literature search was performed and articles identified, reviewed, and assessed for evidence grading. Each topic area was assigned to 2 expert reviewers who developed and presented summaries and recommendations for critique and editing. Furthermore, the Strength of Recommendation Taxonomy, including ratings for the strength of recommendation for a body of evidence, was used throughout for the consensus recommendations for the evaluation and management of pediatric acne. Practical evidence-based treatment algorithms also were developed. Recommendations were put forth regarding the classification, diagnosis, evaluation, and management of pediatric acne, based on age and pubertal status. Treatment considerations include the use of over-the-counter products, topical benzoyl peroxide, topical retinoids, topical antibiotics, oral antibiotics, hormonal therapy, and isotretinoin. Simplified treatment algorithms and recommendations are presented in detail for adolescent, preadolescent, infantile, and neonatal acne. Other considerations, including psychosocial effects of acne, adherence to treatment regimens, and the role of diet and acne, also are discussed. The reviewers concluded the expert recommendations by the American Acne and Rosacea Society as reviewed and endorsed by the American Academy of Pediatrics constitute the first detailed, evidence-based clinical guidelines for the management of pediatric acne including issues of special concern when treating pediatric patients.

Kwon et al (2013) evaluated the efficacy, safety and histological changes of combined blue and red LED phototherapy for acne vulgaris. Thirty-five patients with mild-to-moderate acne were randomly assigned to either a home-use irradiation group using an LED device, or a control group using a sham device. The treatment group was instructed to serially irradiate their forehead and cheeks with 420-nm blue light and 660-nm red light for 2.5 min twice daily for 4 weeks. At the final visit at 12 weeks, both inflammatory and noninflammatory acne lesions had decreased significantly, by 77% and 54%, respectively, in the treatment group. No significant difference was observed in the control group. In the treatment group, sebum output

reduction, attenuated inflammatory cell infiltrations and a decreased size of the sebaceous gland were found. The immunostaining intensities for interleukin (IL)-8, IL-1 α , matrix metalloproteinase-9, toll-like receptor-2, nuclear factor- κ B, insulin-like growth factor-1 receptor and sterol response element binding protein (SREBP)-1 were reduced concomitantly. Messenger RNA expression of SREBP-1c was also decreased. No severe adverse reactions were reported. Investigators concluded LED phototherapy was safe and effective for treating not only inflammatory but also noninflammatory acne lesions, with good compliance. The experimental results correlated well with clinical results, partly elucidating the related molecular mechanisms.

Pinto et al (2013) compared the efficacy and tolerability of red light alone and MAL-PDT in patients with mild to moderate facial acne. Thirty six patients with mild to moderate acne were enrolled. Eighteen patients received MAL-PDT and 18 received red light alone in two sessions, 2 weeks apart. Acne grade and lesion counts were assessed by blinded evaluators at baseline, 2, 4 and 10 weeks. At week 2, clinical improvement from acne grade II-IV to 0-I was observed in 82.3% of MAL-PDT group and 14.2% of red light alone group. Red light alone group had a gradual clinical improvement over time with a 77% response at week 10. In contrast, MAL-PDT group had a rapid clinical improvement with total response at week 10. Both treatments were significantly effective for improving acne lesions. However, MAL-PDT group had a greater response ($P < 0.001$). Histologically, decreased amounts of sebocytes and lipids along with atrophic sebaceous glands were observed after MAL-PDT. Investigators concluded MAL-PDT has a quicker onset of action with a higher response than red light alone. MAL-PDT may induce a reduction in the size of the sebaceous glands and then long-term acne remission.

Scientific Rationale – Update August 2012

Per UpToDate, Dover et al. (2011) The role of laser and other light-based therapies in the treatment of acne is not clearly defined. We suggest that light-based therapies should not be used as first-line treatment for acne vulgaris (Grade 2B*). (Grade 2 recommendation: Weak recommendation, benefits and risks closely balanced and / or uncertain. B notes: Moderate-quality evidence: Evidence from randomized trials with important limitations, or very strong evidence of some other form).

Dréno et al. (2011) completed a study that examines the evidence base that supports the widespread use of superficial peels. Search of the literature revealed very few clinical trials of peels in acne ($N=13$); a majority of these trials included small numbers of patients, were not controlled and were open label. The evidence that is available does support the use of chemical peels in acne as all trials had generally favourable results despite differences in assessments, treatment regimens and patient populations. Notably, no studies of chemical peels have used an acne medication as a comparator. As not every publication specified whether or not concomitant acne medications were allowed, it is hard to evaluate clearly how many of the studies evaluated the effect of peeling alone. This may be appropriate, however, given that few clinicians would use superficial chemical peels as the sole treatment for acne except in rare instances where a patient could not tolerate other treatment modalities. In the future, further study is needed to determine the best use of chemical peels in this indication.

There was a paucity of studies on dermabrasion and cryotherapy for acne treatment. Therefore, at this time, phototherapy, laser therapy, chemical peels, dermabrasion and cryotherapy for acne treatments continue to be considered investigational.

Scientific Rationale – Update January 2011

A variety of therapeutic options to treat acne vulgaris continue to be investigated in the published literature. Orringer et al (2010) conducted a randomized, controlled, split-face, single-blind clinical trial of 44 patients with facial acne. Patients were randomized to receive three pulsed dye laser treatments to one side of the face after a 60-90 min ALA application time, while the contralateral side remained untreated and served as a control. Serial blinded lesion counts and global acne severity ratings were performed. Global acne severity ratings improved bilaterally with the improvement noted to be statistically significantly greater in treated skin than in untreated skin. Erythematous macules (remnants of previously active inflammatory lesions) decreased in number in treated skin when compared with control skin and there was a transient but significant decrease in inflammatory papules in treated skin when compared with untreated skin. There were no other statistically significant differences between treated and untreated sides of the face in terms of counts of any subtype of acne lesion. Thirty percent of patients were deemed responders to this treatment with respect to improvement in their inflammatory lesion counts, while only 7% of patients responded in terms of noninflammatory lesion counts. The investigators concluded PDT with the treatment regimen employed here may be beneficial for a subgroup of patients with inflammatory acne.

de Arruda et al (2009) evaluated the efficacy and safety of blue light treatment versus topical benzoyl peroxide 5% formulation in 60 patients with acne grades II and III. Patients were evaluated in 5 visits: the first one for screening, another 3 held on days 7, 14 and 28 of treatment, and the last one after 14 days of the end of treatment. Thirty of them were irradiated with Blue Light (8 times, twice a week) and the other thirty were treated with topical Benzoyl Peroxide 5% formulation, auto-applied twice a day, every day. The severity of acne was assessed by counting the lesions and analyzing the photographs. The improvement achieved by the blue light was the same as the one with benzoyl peroxide, regardless of the type of lesion ($p < 0.05$). Otherwise, the side effects were less frequent in the group treated with blue light. The investigators concluded blue light irradiation was as effective as benzoyl peroxide in acne treatment grades II and III but there were fewer side effects.

Choi et al (2010) investigated twenty patients with facial acne treated using intense pulsed light (IPL) on one side of the face and pulsed dye laser (PDL) on the other comparing the efficacy and safety of IPL and PDL. Treatment was performed 4 times at 2-week intervals. Treatment effectiveness was determined using lesion counts, acne severity, patient subjective self-assessments of improvement, and histopathological examinations, which included immunohistochemical staining for transforming growth factor-beta (TGF-beta). Numbers of total acne lesions decreased following both treatments. For inflammatory lesions such as papules, pustules and nodules, IPL-treated sides showed an earlier and more profound improvement than PDL-treated sides. However, at 8 weeks after the 4th treatment, a rebound aggravation of acne was observed on IPL-treated sides. On the contrary, PDL produced gradual improvements during the treatment sessions and these improvements lasted 8 weeks after the 4th treatment. Non-inflammatory lesions as open and closed comedones also showed improvement following both treatments and PDL-treated sides showed better improvement as the study proceeded. Histopathological examinations showed amelioration in inflammatory reactions and an increase in TGF-beta expression after both treatments, which were more prominent for PDL-treated sides. The investigators concluded both PDL and IPL were found to treat acne effectively, but PDL showed a more sustained effect. TGF-beta might play a key role in the resolution of inflammatory acne lesions.

Hamilton et al (2009) performed a systematic review of randomized controlled trials of light and laser therapies for acne vulgaris. 25 trials (694 patients) were identified,

13 of light therapy and 12 of light therapy plus light-activated topical cream (photodynamic therapy, PDT). The reviewers noted that overall, the results from trials of light alone were disappointing, but the trials of blue light, blue-red light and infrared radiation were more successful, particularly those using multiple treatments. Red-blue light was more effective than topical 5% benzoyl peroxide cream in the short term. Most trials of PDT showed some benefit, which was greater with multiple treatments, and better for noninflammatory acne lesions. However, the improvements in inflammatory acne lesions were not better than with topical 1% adapalene gel, and the side-effects of therapy were unacceptable to many participants. The reviewers concluded some forms of light therapy were of short-term benefit. Patients may find it easier to comply with these treatments, despite the initial discomfort, because of their short duration. However, very few trials compared light therapy with conventional acne treatments, were conducted in patients with severe acne or examined long-term benefits of treatment.

Scientific Rationale

Acne vulgaris is the most common cutaneous disorder in the United States. It is estimated that 85 percent of the adolescent population experiences this condition and the number of patients over the age of 25 with either late onset or persistent acne vulgaris is increasing.

Acne vulgaris is a chronic inflammatory dermatosis notable for open and/or closed comedones (blackheads and whiteheads) and inflammatory lesions including papules, pustules, or nodules. Scarring and hyperpigmentation can occur. Acne typically affects those areas of the body that have the greatest number of sebaceous glands, including the face, neck, chest, upper back, and upper arms. In 1990, the American Academy of Dermatology (AAD) developed a classification scheme for primary acne vulgaris. This grading scale delineates three levels of acne: mild, moderate, and severe. Mild acne is characterized by the presence of few to several papules and pustules, but no nodules. Patients with moderate acne have several to many papules and pustules, along with a few to several nodules. With severe acne, patients have numerous or extensive papules and pustules, as well as many nodules. Acne also is classified by type of lesion-comedonal, papulopustular, and nodulocystic. Pustules and cysts are considered inflammatory acne.

The goals of acne therapy include controlling acne lesions, preventing scarring and minimizing morbidity. The choice of acne therapy is determined by several factors including the major type of acne lesion present, severity and extent of the condition, response to previous therapies, concurrent medical treatments and conditions and patient-physician choice in therapeutic modalities based on personal and lifestyle choices. Topical agents such as topical retinoids, benzoyl peroxide, and topical antibiotics represent the mainstay of therapy for mild and moderate acne. Patients who have mild disease may be cleared successfully with topical therapy alone, whereas those who have moderate acne may require topical therapy in conjunction with systemic medications. Systemic antibiotic therapy is typically indicated for moderate to severe inflammatory disease. Tetracycline and its derivatives (e.g. Doxycycline, Minocycline) are the preferred oral antibiotic choice for acne. Adjunctive therapy in female patients include oral contraceptives and spironolactone. Long-term topical or oral antibiotic therapy should be avoided when feasible to minimize occurrence of bacterial resistance.

Oral retinoids (isotretinoin) may also be used for the treatment of severe recalcitrant nodular acne or management of lesser degrees of acne that are treatment-resistant. Isotretinoin (e.g. Accutane) is a systemic retinoid and represents the single most effective therapeutic agent for the treatment of nodulocystic acne, however, oral isotretinoin is a potent teratogen. The FDA has approved the iPledge Program, a risk

management program for isotretinoin, designed to eliminate fetal exposure to isotretinoin through a special restricted distribution program, established jointly by the manufacturers of the drug. Prescribers, patients, pharmacies, drug wholesalers, and manufacturers in the United States are required to register and comply with the iPLEDGE program. This program requires mandatory registration of all patients receiving this drug. Detailed information can be found on the iPLEDGE web site.

Acne surgery involves the removal of non-inflamed acne lesions. It includes the opening up of comedones (blackheads and whiteheads) and pimples using a needle or small pointed blade and the expressing of the lesions with an extractor. Individual acne lesions, especially those lesions unresponsive to traditional therapy, may require treatment directly to the affected area to reduce pain, swelling and subsequent scarring. Acne surgery may include such treatments as extraction of comedonal contents, incision and drainage of pustules and cysts, and excision of cysts. According to the AAD "Guidelines of care for acne vulgaris management" (2007) "There is limited evidence published in peer reviewed medical literature that addresses the efficacy of comedo removal for the treatment of acne, despite its long-standing clinical use. Comedo removal may be helpful in the management of comedones resistant to other therapies."

In conjunction with other treatments, intralesional injection may be used for individual nodulocystic and large pustular lesions. Occasionally, intralesional steroid injections may be given for small papules and pustules when rapid resolution is desired. According to the AAD guideline, intralesional injection with corticosteroids is a well-established and recognized treatment for large inflammatory lesions.

According to the AAD, there is limited evidence regarding the benefit of physical modalities including glycolic acid and salicylic acid peels, however, both glycolic acid-based and salicylic acid-based peeling preparations have been used in the treatment of acne. Per the AAD guideline "There is very little evidence from clinical trials published in the peer-reviewed literature supporting the efficacy of peeling regimens (chemical peels.) Further research on the use of peeling in the treatment of acne needs to be conducted in order to establish best practices for this modality."

Cryosurgery is a procedure utilizing cryogenic agents to treat a variety of cutaneous diseases. Freezing temperatures of a cryogenic agent, applied directly or indirectly to the skin cause local destruction of tissue. Cryotherapy with liquid nitrogen or cryoslush therapy mixing solid carbon dioxide and acetone have been used in the treatment of active acne. Light freezing causes a peeling, moderate freezing a blistering and hard freezing a scabbing. Cryoablation of the skin for acne is of questionable efficacy and is rarely indicated.

The AAD defines phototherapy as exposure to nonionizing radiation for therapeutic benefit. It may involve exposure to UVB, UVA or various combinations of UVB and UVA radiation. The objective of phototherapy (light therapy) for acne vulgaris is to destroy *Propionibacterium acnes* (*P. acnes*), the bacterium associated with the production of inflammatory acne lesions, thereby promoting the resolution of existing acne lesions. Visible light phototherapy utilizes ultraviolet-free light within the visible spectrum, such as blue and red visible light, with wavelengths spanning 415 to 660 nm. High-intensity narrow-band blue light (405 to 420 nm) therapy (i.e., ClearLight) is approved by the US FDA for treatment of moderate inflammatory acne. Clearlight is a high intensity lamp intended for the treatment of acne vulgaris by emitting visible light in the violet-blue range. It is thought that the violet-blue spectrum of high-intensity light triggers the proliferation of endogenous porphyrins, which attack and destroy the acne bacteria within the skin.

Noborio et al. (2007) evaluated a new blue light system (MultiClear) for targeted blue light phototherapy in ten patients with acne on the face or back. Patients were treated once or twice a week, of the 10 patients, eight had a significantly reduced acne severity score without any side effects. Although two patients discontinued the study because of unsatisfactory results, none of the patients showed any harmful side effects from the targeted blue light phototherapy. The investigator concluded targeted blue light phototherapy with MultiClear is effective for the treatment of inflammatory acne lesions.

Goldberg et al. (2006) assessed the efficacy of this combination phototherapy with combination blue (415 nm) and red (633 nm) LED phototherapy. The study included twenty-four patients with mild to severe symmetric facial acne vulgaris. Patients were treated over eight sessions, two per week 3 days apart, alternating between 415 nm blue light and 633 nm red light from a light-emitting diode (LED)-based therapy system. Patients received a mild microdermabrasion before each session. Acne was assessed at baseline and at weeks 2, 4, 8 and 12. Twenty-two patients completed the trial. A mean reduction in lesion count was observed at all follow-up points. At the 4-week follow-up, the mean lesion count reduction was significant at 46%. At the 12-week follow-up, the mean lesion count reduction was also significant at 81%. Patient and dermatologist assessments were similar. Severe acne showed a marginally better response than mild acne. Side effects were minimal and transitory. Comedones did not respond as well as inflammatory lesions. The investigator concluded combination blue and red LED therapy appears to have excellent potential in the treatment of mild to severe acne. Treatment appears to be both pain- and side effect-free.

Kawada et al. (2002) reported that in a small uncontrolled trial of twice weekly therapy with ClearLight (407 to 420 nm), patients with mild to moderate acne treated for up to five weeks had a 64 percent reduction in acne lesions.

Further data are needed from large randomized controlled clinical trials before visible light phototherapy can be recommended for the treatment of acne.

Photodynamic Therapy is characterized by the use of visible light in addition to a topical application of a photosensitizer, such as a commonly used agent, 5-aminolevulinic acid (ALA) and recently methyl aminolevulinate. In 1999, the Levulan Kerastick for topical solution plus blue light illumination using the BLU-U Blue Light Photodynamic Therapy Illuminator, received approval by the U.S. Food and Drug Administration (FDA) for the treatment of non-hyperkeratotic actinic keratoses (AK) of the face and scalp." As described in the package insert, the technique involves two steps starting with application of the ALA Topical Solution in the physician's office. 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.

Photodynamic therapy (PDT) in addition to a topical application of a photosensitizer, such as a commonly used agent, 5-aminolevulinic acid (ALA) or methyl aminolevulinate has also been proposed as a treatment of persistent acne as well as cosmetic procedures such as photo rejuvenation. For the treatment of acne, this technique differs slightly than that of treatment of AK. It involves the application of Levulan Kerastick topical solution to the acne which is left on the skin for 45-60 minutes, followed by a blue light treatment session lasts 4-8 minutes. Photodynamic

therapy using ALA may be associated with pain, erythema, edema, and hyper- or hypopigmentation.

Published studies are limited regarding the use of ALA and Photodynamic therapy (PDT) in the treatment of acne. There also lacks published studies comparing ALA-PDT to standard treatment of acne vulgaris. Preliminary evidence suggests that photodynamic therapy and ALA may significantly improve acne symptoms, but the sample size and the number of studies are too small to determine efficacy and safety. One such example is that of a small published study of 18 patients (Taub, 2004) with moderate to severe inflammatory acne, treated with ALA for 15 to 30 minutes before exposure to blue light, reported improvement in 12 patients (11 had at least 50% improvement and five had more than 75% improvement) after two to four ALA-PDT treatments over four to eight weeks or two cycles of ALA-PDT (weeks 2, 4) preceded by salicylic acid peel (weeks 1, 3) over four weeks. The average follow-up time was four months.

Gold et al. (2007) evaluated the safety and efficacy of a new Advanced Fluorescence Technology (AFT) pulsed light source (420-950 nm) for photoactivation in ALA PDT for the treatment of moderate to severe inflammatory facial acne vulgaris. Nineteen patients received 4 ALA PDT treatments with the AFT pulsed light source, spaced 2 weeks apart. ALA was incubated for 15 to 30 minutes. At the end of the fourth treatment, the total reductions in inflammatory and non-inflammatory lesion counts were 54.5% and 37.5%, respectively. Investigator and patient assessments show moderate to marked improvement were noted in most patients by the investigator and patient assessment. The investigator concluded the new AFT pulsed light source with ALA PDT appears to be a safe and effective modality for the treatment of moderate to severe inflammatory acne vulgaris.

Wiegell et al. (2006) evaluated the efficacy and tolerability of methyl aminolaevulinate-based photodynamic therapy (MAL-PDT) in patients with moderate to severe facial acne vulgaris in a randomized, controlled and investigator-blinded trial. Twenty-one patients were assigned to the treatment group and 15 patients to the control group. The treatment group received two MAL-PDT treatments, 2 weeks apart. Both groups were evaluated 4, 8 and 12 weeks after treatment. Twelve weeks after treatment the treatment group showed a 68% reduction from baseline in inflammatory lesions vs. no change in the control group. No reduction in number of noninflammatory lesions were found after treatment. All patients experienced moderate to severe pain during treatment and developed severe erythema, pustular eruptions and epithelial exfoliation. Seven patients did not receive the second treatment due to adverse effects. The investigator concluded MAL-PDT proved to be an efficient treatment for inflammatory acne but was associated with severe pain during treatment and severe adverse effects after treatments.

Wiegell et al. (2006) also compared the treatment effect of aminolevulinic acid-PDT (ALA-PDT) and methyl aminolevulinate-PDT (MAL-PDT). In this randomized trial, fifteen patients with at least 12 facial inflammatory acne lesions had one split-face PDT treatment with MAL and ALA. Twelve weeks after treatment we found a 59% decrease in inflammatory lesions from baseline, with no significant differences in effectiveness between the two treatments. All patients experienced moderate to severe pain during illumination and developed erythema, pustular eruptions, and epithelial exfoliation after treatment, which were more severe and uniform in the ALA-PDT-treated area. The investigator concluded that PDT appeared to be an effective treatment for inflammatory acne vulgaris with no significant differences in the response rate between ALA-PDT and MAL-PDT. ALA-PDT resulted in more prolonged and severe adverse effects after treatment.

At this time, due to lack of well-designed controlled studies with large sample size and long-term, follow-up, as well as a lack of studies comparing this treatment to that of standard treatment of acne, we consider this treatment for acne investigational at this time. There is insufficient evidence to recommend photodynamic therapy with topical ALA or MAL and exposure to blue light in the treatment of acne vulgaris.

Lasers investigated in the treatment of inflammatory acne vulgaris include the 532-nm potassium titanyl phosphate laser, 585- and 595-nm pulsed dye lasers, 1450-nm diode laser, and 1540-nm erbium glass laser. There have been a number of recently published studies, however, they have been small and have not included comparisons with established treatments for acne vulgaris.

Orringer et al. (2007) examine the efficacy of an infrared laser in the treatment of acne in a randomized, controlled, single-blind, split-face clinical trial of 46 patients with facial acne. Patients received a series of 3 nonablative laser treatments using a novel neodymium:yttrium-aluminum-garnet (Nd:YAG) laser to half of the face. Serial blinded lesion counts and global acne severity rating of standardized bilateral patient photographs were performed. Sebum production was measured, and patient self-assessment surveys were administered. A transient but statistically significant improvement in lesion counts of open comedones was demonstrated in treated skin as compared with untreated skin. There were no significant differences between treated and control sides of the face in terms of changes in mean papule or pustule counts. Grading of serial photographs revealed no significant differences between treated and untreated skin. Patient surveys indicated that the majority of patients found the treatments to be at least mildly effective for both acne and oiliness. The investigators noted this study only addresses the efficacy of a single laser system employing a specific treatment regimen. The investigators reported infrared laser therapy may improve comedonal acne although additional work is needed to better define the degree and duration of the effect. Patients appear to positively view such therapy for both acne and oily skin.

Baugh et al. (2005) investigated the safety and efficacy of the potassium titanyl phosphate (KTP) 532 nm pulsed laser for the treatment of acne vulgaris. Twenty-six patients with moderate facial acne, were enrolled in this single-center prospective trial. The entire facial area for each subject was divided in half and randomly designated as either a treatment or a control side. Each subject was treated with four laser exposures using a KTP 532 nm laser with continuous contact cooling. The results were assessed at 1 and 4 weeks post-final treatment. Primary outcome measures were Michaëlsson acne severity score and adverse treatment effects. Secondary outcome measures included subjective evaluations from the investigator and patients assessing their overall percent satisfaction. Primary outcome analysis in the Michaëlsson acne severity score demonstrated a mean 34.9% and 20.7% reduction at the 1-week and 4-week post-final treatments, respectively. Subjective investigator evaluations of overall percent satisfaction indicated that all patients demonstrated a minimum 50% overall satisfaction in treatment outcomes at the 4-week follow-up period. No side effects were encountered. The investigator concluded the use of the KTP 532 nm laser for the treatment and management of acne vulgaris is both safe and effective, with positive results enduring up to 4 weeks post-treatment.

A Cochrane review assessed the effects of laser resurfacing for treating facial acne scars from randomised controlled trials which compare different laser resurfacing techniques for treating patients with facial acne scars, or compare laser resurfacing with other resurfacing techniques or no treatment. No randomised controlled trials where laser treatment was compared to either placebo or a different type of laser

were found. Most of the 27 studies uncovered were poor quality case series with small numbers of acne-scarred patients. The reviewers concluded the lack of good quality evidence does not enable any conclusions to be drawn about the effectiveness of lasers for treating atrophic or ice-pick acne scars. Well designed randomised controlled comparisons of carbon dioxide versus Erbium:YAG laser are urgently needed. The efficacy of laser treatment is still uncertain, there remains a need for long-term data and randomized, blinded studies.

Chemical peels, lasers, and dermabrasion are among the most common modalities used for cosmetic improvement of facial scars. Facial dermabrasion is a mechanical method using abrasive surfaces to remove the epidermis and create a wound in the papillary or reticular dermis. This subsequently causes the stimulation of type I and III collagen and formation of a fresh new layer of skin. Facial dermabrasion is most commonly used for the treatment facial scars induced by acne, varicella, or removal of superficial skin lesions and removal of wrinkles.

Microdermabrasion uses the abrasive action of small particle microcrystals (i.e., aluminum oxide, sodium chloride, or sodium bicarbonate) to wound the epidermis, coupled with suction to remove any skin debris. An inflammatory response is stimulated within the epidermis and results in the formation of a new stratum corneum within 3 to 5 days. Typically, a series of treatments are required to achieve the desired resurfacing results (6 to 10 treatments), followed by a maintenance program every 4 to 6 weeks. Microdermabrasion is most often used for epidermal conditions including fine rhytids, dyschromia, superficial scarring from acne and actinic keratosis. Widespread active acne should be viewed as a contraindication to microdermabrasion.

Acne responses to treatment vary considerably. Frequently more than one treatment modality is used concomitantly. Best results are seen when treatments are individualized on the basis of clinical presentation. Research emphasizing long-term follow-up and comparative, randomized trials is necessary to determine whether emerging technologies will become a viable alternative to standard therapies.

Review History

August 2007	Medical Advisory Council initial approval
August 2008	CA reconstructive surgery law added to Disclaimer
January 2011	Update – no revisions
September 2011	Update – no revisions
August 2012	Update – no revisions
August 2013	Update – no revisions. Code updates.
August 2014	Update – no revisions
August 2015	Update – no revisions

This policy is based on the following evidence-based guidelines:

1. Strauss JS, Krowchuk DP, Leyden JJ, et al. American Academy of Dermatology/ American Academy of Dermatology Association. Guidelines of care for acne vulgaris management. J Am Acad Dermatol. 2007 Apr;56(4):651-63. (guideline archived)
2. Institute for Clinical Systems Improvement (ICSI). Acne management. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 May.
3. American Academy of Dermatology (AAD). Position Statement on Acne. March 2000.
4. Hayes Medical Technology Directory. Phototherapy for Acne Vulgaris. Dec. 2005. Updated Jan 2010, 2012. Updated Jan 2013. Archived Mar 2014

5. Hayes Alert – TechnologyAssessment Brief. Photodynamic Therapy for Acne Vulgaris. Volume VIII, Number 8 –August 2005
6. American Academy of Dermatologists (AAD). Guidelines of Care for Phototherapy and Photochemotherapy. J Am Acad Dermatol 1994;31:643-8.
7. Eichenfield LF, Krakowski AC, Piggott C, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. Pediatrics. 2013 May;131 Suppl 3:S163-86. Available at: http://pediatrics.aappublications.org/content/131/Supplement_3/S163.full.pdf+html?sid=da14e9a1-e7d6-4de8-9fec-15d84bbf23fd

References – Update August 2015

1. Ash C, Harrison A, Drew S, Whittall R. A randomized controlled study for the treatment of acne vulgaris using high-intensity 414 nm solid state diode arrays. J Cosmet Laser Ther. 2015 Feb 20:1-7.
2. Bhate K, Williams HC. What's new in acne? An analysis of systematic reviews published in 2011-2012. Clin Exp Dermatol. 2014 Apr;39(3):273-7
3. Dong Y, Zhou G, Chen J, et al. A new LED device used for photodynamic therapy in treatment of moderate to severe Acne vulgaris. Photodiagnosis Photodyn Ther. 2015 Jun 23.
4. Kim HW, Chang SE, Kim JE, et al. The safe delivery of fractional ablative carbon dioxide laser treatment for acne scars in Asian patients receiving oral isotretinoin. Dermatol Surg. 2014 Dec;40(12):1361-6.
5. Ma Y, Liu Y, Wang Q, Ren J, Xiang L. Prospective study of topical 5-aminolevulinic acid photodynamic therapy for the treatment of severe adolescent acne in Chinese patients. J Dermatol. 2015 May;42(5):504-7.
6. Moneib H, Tawfik AA, Youssef SS, Fawzy MM. Randomized split-face controlled study to evaluate 1550-nm fractionated erbium glass laser for treatment of acne vulgaris--an image analysis evaluation. Dermatol Surg. 2014 Nov;40(11):1191-200.
7. Song BH, Lee DH, Kim BC, et al. Photodynamic therapy using chlorophyll-a in the treatment of acne vulgaris: a randomized, single-blind, split-face study. J Am Acad Dermatol. 2014 Oct;71(4):764-71

References – Update August 2014

1. Bartlett KB, Davis SA, Feldman SR. Tolerability of topical antimicrobials in treatment of acne vulgaris. Drugs Dermatol. 2014 Jun 1;13(6):658-62.
2. Bhate K, Williams HC. What's new in acne? An analysis of systematic reviews published in 2011-2012. Clin Exp Dermatol. 2014 Apr;39(3):273-7.
3. Garg S, Baveja S. Combination therapy in the management of atrophic acne scars. J Cutan Aesthet Surg. 2014 Jan;7(1):18-23.
4. Koo EB, Petersen TD, Kimball AB. Meta-analysis comparing efficacy of antibiotics versus oral contraceptives in acne vulgaris. J Am Acad Dermatol. 2014 May 28. pii: S0190-9622(14)01291-2.
5. Linkner RV, Jim On S, Haddican M, et al. Evaluating the Efficacy of Photodynamic Therapy with 20% Aminolevulinic Acid and Microdermabrasion as a Combination Treatment Regimen for Acne Scarring: A Split-face, Randomized, Double-blind Pilot Study. J Clin Aesthet Dermatol. 2014 May;7(5):32-5.
6. Lynde C, Tan J, Andriessen A, et al. A consensus on acne management focused on specific patient features. J Cutan Med Surg. 2014 Apr;18:1-13.
7. Song BH, Lee DH, Kim BC, et al. Photodynamic therapy using chlorophyll-a in the treatment of acne vulgaris: A randomized, single-blind, split-face study. J Am Acad Dermatol. 2014 Jun 12.

References – Update August 2013

1. Calzavara-Pinton PG, Rossi MT, Aronson E, et al. A retrospective analysis of real-life practice of off-label photodynamic therapy using methyl aminolevulinic acid (MAL-PDT) in 20 Italian dermatology departments. Part 1: inflammatory and aesthetic indications. *Photochem Photobiol Sci*. 2013 Jan;12(1):148-57.
2. Erceg A, de Jong EM, van de Kerkhof PC, Seyger MM. The efficacy of pulsed dye laser treatment for inflammatory skin diseases: A systematic review. *J Am Acad Dermatol*. 2013 May 24
3. Fulton J. Acne Vulgaris. Medscape - Updated May 2013. Available at: <http://emedicine.medscape.com/article/1069804-treatment>
4. Handog EB, Datuin MS, Singzon IA. Chemical peels for acne and acne scars in Asians: evidence based review. *Cutan Aesthet Surg*. 2012 Oct;5(4):239-46.
5. Kostović K, Pastar Z, Ceović R, et al. Photodynamic therapy in dermatology: current treatments and implications. *Coll Antropol*. 2012 Dec;36(4):1477-81.
6. Kwon HH, Lee JB, Yoon JY, et al. The clinical and histological effect of home-use, combination blue-red LED phototherapy for mild-to-moderate acne vulgaris in Korean patients: a double-blind, randomized controlled trial. *Br J Dermatol*. 2013 May;168(5):1088-94.
7. Qian H, Lu Z, Ding H, et al. Treatment of acne scarring with fractional CO2 laser. *J Cosmet Laser Ther*. 2012 Aug;14(4):162-5.
8. Pinto C, Schafer F, Orellana JJ, et al. Efficacy of red light alone and methylaminolevulinic acid-photodynamic therapy for the treatment of mild and moderate facial acne. *Indian J Dermatol Venereol Leprol*. 2013 Jan-Feb;79(1):77-82.
9. Wang HW, Lv T, Zhang LL, et al. Prospective study of topical 5-aminolevulinic acid photodynamic therapy for the treatment of moderate to severe acne vulgaris in Chinese patients. *J Cutan Med Surg*. 2012 Sep-Oct;16(5):324-33.

References – Update August 2012

1. Dover JS, Batra P. Light-based adjunctive, and other therapies for acne vulgaris. *UpToDate*. 2011.
2. Dréno B, Fischer TC, Perosino E, et al. Expert opinion: efficacy of superficial chemical peels in active acne management--what can we learn from the literature today? Evidence-based recommendations. *J Eur Acad Dermatol Venereol*. 2011 Jun;25(6):695-704. Epub 2010 Oct 3.
3. Graber E. Treatment of acne vulgaris. *UpToDate*. April 13, 2012.
4. Levesque A, Hamzavi I, Seife S, et al. Randomized trial comparing a chemical peel containing a lipophilic hydroxy acid derivative of salicylic acid with a salicylic acid peel in subjects with comedonal acne. *J Cosmet Dermatol*. 2011 Sep; 10(3):174-8.

References – Update September 2011

1. Carniol PJ, Meshkov L, Grunebaum LD. Laser treatment of facial scars. *Curr Opin Otolaryngol Head Neck Surg*. 2011 Jun 8
2. Feneran AN, Kaufman WS, Dabade TS, Feldman SR. Retinoid plus antimicrobial combination treatments for acne. *Clin Cosmet Investig Dermatol*. 2011;4:79-92
3. Isarría MJ, Cornejo P, Muñoz E, et al. Evaluation of Clinical Improvement in Acne Scars and Active Acne in Patients Treated With the 1540-nm Non-Ablative Fractional Laser. *J Drugs Dermatol*. 2011 Aug 1;10(8):907-12.
4. Kim RH, Armstrong AW. Current state of acne treatment: highlighting lasers, photodynamic therapy, and chemical peels. *Dermatol Online J*. 2011 Mar 15;17(3):2
5. Webster GF. Evidence-based review: fixed-combination therapy and topical retinoids in the treatment of acne. *Drugs Dermatol*. 2011 Jun 1;10(6):636-44.

References – Update January 2011

1. Arowojolu AO, Gallo MF, Lopez LM, et al. Combined oral contraceptive pills for treatment of acne. *Cochrane Database Syst Rev*. 2009 Jul 8;(3):CD004425
2. Choi YS, Suh HS, Yoon MY, et al. 10-Intense pulsed light vs. pulsed-dye laser in the treatment of facial acne: a randomized split-face trial. *J Eur Acad Dermatol Venereol*. 2010 Jul;24(7):773-80
3. de Arruda LH, Kodani V, Bastos Filho A, Mazzaro CB. A prospective, randomized, open and comparative study to evaluate the safety and efficacy of blue light treatment versus a topical benzoyl peroxide 5% formulation in patients with acne grade II and III. *An Bras Dermatol*. 2009 Oct;84(5):463-8.
4. Eichenfield LF, Jarratt M, Schlessinger J, et al. Adapalene 0.1% lotion in the treatment of acne vulgaris: results from two placebo-controlled, multicenter, randomized double-blind, clinical studies. *J Drugs Dermatol*. 2010 Jun;9(6):639-46.
5. Hamilton FL, Car J, Lyons C, et al. Laser and other light therapies for the treatment of acne vulgaris: systematic review. *Br J Dermatol*. 2009 Jun;160(6):1273-85.
6. Jackson JM, Fu JJ, Almekinder JL. A randomized, investigator-blinded trial to assess the antimicrobial efficacy of a benzoyl peroxide 5%/ clindamycin phosphate 1% gel compared with a clindamycin phosphate 1.2%/tretinoin 0.025% gel in the topical treatment of acne vulgaris. *J Drugs Dermatol*. 2010 Feb;9(2):131-6.
7. Fleischer AB Jr, Shalita A, Eichenfield LF, et al. Dapsone gel 5% in combination with adapalene gel 0.1%, benzoyl peroxide gel 4% or moisturizer for the treatment of acne vulgaris: a 12-week, randomized, double-blind study. *J Drugs Dermatol*. 2010 Jan;9(1):33-40.
8. Lee JW, Yoo KH, Park KY, et al. Effectiveness of Conventional, Low-dose and Intermittent Oral Isotretinoin in the Treatment of Acne: A Randomized, Controlled Comparative study. *Br J Dermatol*. 2010 Nov 29.
9. Nilfroushzadeh MA, Siadat AH, Baradaran EH, Moradi S. Clindamycin lotion alone versus combination lotion of clindamycin phosphate plus tretinoin versus combination lotion of clindamycin phosphate plus salicylic acid in the topical treatment of mild to moderate acne vulgaris: a randomized control trial. *Indian J Dermatol Venereol Leprol*. 2009 May-Jun;75(3):279-82.
10. Orringer JS, Sachs DL, Bailey E, et al. Photodynamic therapy for acne vulgaris: a randomized, controlled, split-face clinical trial of topical aminolevulinic acid and pulsed dye laser therapy. *J Cosmet Dermatol*. 2010 Mar;9(1):28-34.
11. Sadick N. An open-label, split-face study comparing the safety and efficacy of levulan kerastick (aminolevulinic acid) plus a 532 nm KTP laser to a 532 nm KTP laser alone for the treatment of moderate facial acne. *J Drugs Dermatol*. 2010 Mar;9(3):229-33.
12. Seidler EM, Kimball AB. Meta-analysis comparing efficacy of benzoyl peroxide, clindamycin, benzoyl peroxide with salicylic acid, and combination benzoyl peroxide/clindamycin in acne. *J Am Acad Dermatol*. 2010 Jul;63(1):52-62
13. Tanghetti E, Dhawan S, Green L, et al. Randomized comparison of the safety and efficacy of tazarotene 0.1% cream and adapalene 0.3% gel in the treatment of patients with at least moderate facial acne vulgaris. *J Drugs Dermatol*. 2010 May;9(5):549-58.
14. Yentzer BA, Ade RA, Fountain JM, et al. Simplifying regimens promotes greater adherence and outcomes with topical acne medications: a randomized controlled trial. *Cutis*. 2010 Aug;86(2):103-8.

References

1. Gold MH, Biron JA, Boring M, et al. Treatment of moderate to severe inflammatory acne vulgaris: photodynamic therapy with 5-aminolevulinic acid and a novel advanced fluorescence technology pulsed light source. *J Drugs Dermatol*. 2007 Mar;6(3):319-22.

2. Lee SY, You CE, Park MY. Blue and red light combination LED phototherapy for acne vulgaris in patients with skin phototype IV. *Lasers Surg Med.* 2007 Feb;39(2):180-8.
3. Nestor MS. The use of photodynamic therapy for treatment of acne vulgaris. *Dermatol Clin.* 2007 Jan;25(1):47-57.
4. Perez-Maldonado A, Runger TM, Krejci-Papa N. The 1,450-nm diode laser reduces sebum production in facial skin: a possible mode of action of its effectiveness for the treatment of acne vulgaris. *Lasers Surg Med.* 2007 Feb;39(2):189-92
5. Noborio R, Nishida E, Kurokawa M, Morita A. A new targeted blue light phototherapy for the treatment of acne. *Photodermatol Photoimmunol Photomed.* 2007 Feb;23(1):32-4.
6. Orringer JS, Kang S, Maier L, et al. A randomized, controlled, split-face clinical trial of 1320-nm Nd:YAG laser therapy in the treatment of acne vulgaris. *J Am Acad Dermatol.* 2007 Mar;56(3):432-8.
7. Yeung CK, Shek SY, Bjerring P. et al. A comparative study of intense pulsed light alone and its combination with photodynamic therapy for the treatment of facial acne in Asian skin. *Lasers Surg Med.* 2007 Jan;39(1):1-6.
8. Alexiades-Armenakas M. Long-pulsed dye laser-mediated photodynamic therapy combined with topical therapy for mild to severe comedonal, inflammatory, or cystic acne. *J Drugs Dermatol.* 2006 Jan;5(1):45-55.
9. Babilas P, Landthaler M, Szeimies RM. Photodynamic therapy in dermatology. *Eur J Dermatol.* 2006 Sep;16(4):340-8
10. Bhatia AC, Dover JS, Arndt KA et al. Patient satisfaction and reported long-term therapeutic efficacy associated with 1,320 nm Nd:YAG laser treatment of acne scarring and photoaging. *Dermatol Surg.* 2006 Mar;32(3):346-52
11. Glaich AS, Friedman PM, Jih MH, Goldberg LH. Treatment of inflammatory facial acne vulgaris with combination 595-nm pulsed-dye laser with dynamic-cooling-device and 1,450-nm diode laser. *Lasers Surg Med.* 2006 Mar;38(3):177-80
12. Goldberg DJ, Russell BA. Combination blue (415 nm) and red (633 nm) LED phototherapy in the treatment of mild to severe acne vulgaris. *J Cosmet Laser Ther.* 2006 Jun;8(2):71-5.
13. Horfelt C, Funk J, Frohm-Nilsson M, et al. Topical methyl aminolaevulinate photodynamic therapy for treatment of facial acne vulgaris: results of a randomized, controlled study. *Br J Dermatol.* 2006 Sep;155(3):608-13.
14. Jury CS, McHenry P, Burden AD, Lever R, Bilsland D. Narrowband ultraviolet B (UVB) phototherapy in children. *Clin Exp Dermatol.* 2006 Mar;31(2):196-9.
15. Lee SH, Huh CH, Park KC, Youn SW. Effects of repetitive superficial chemical peels on facial sebum secretion in acne patients. *J Eur Acad Dermatol Venereol.* 2006 Sep;20(8):964-8.
16. Leyden, JJ, Krochmal, L, Yaroshinsky, A. Two randomized, double-blind, controlled trials of 2219 subjects to compare the combination clindamycin/tretinoin hydrogel with each agent alone and vehicle for the treatment of acne vulgaris. *J Am Acad Dermatol* 2006 Jan;54(1):73-81
17. Nouri K, Ballard CJ. Laser therapy for acne. *Clin Dermatol.* 2006 Jan-Feb;24(1):26-32. Wiegell SR, Wulf HC. Photodynamic therapy of acne vulgaris using methyl aminolaevulinate: a blinded, randomized, controlled trial. *Br J Dermatol.* 2006 May;154(5):969-76.
18. Wiegell SR, Wulf HC. Photodynamic therapy of acne vulgaris using methyl aminolaevulinate: a blinded, randomized, controlled trial. *Br J Dermatol.* 2006 May;154(5):969-76.
19. Wiegell SR, Wulf HC. Photodynamic therapy of acne vulgaris using 5-aminolevulinic acid versus methyl aminolevulinate. *J Am Acad Dermatol.* 2006 Apr;54(4):647-51
20. Yan AC. Current concepts in acne management. *Adolesc Med Clin.* 2006 Oct; 17(3): 613-37; abstract x-xi

21. Zakopoulou N, Kontochristopoulos G. Superficial chemical peels. *J Cosmet Dermatol*. 2006 Sep;5(3):246-53.
22. Baugh WP, Kucaba WD. Nonablative phototherapy for acne vulgaris using the KTP 532 nm laser. *Dermatol Surg*. 2005 Oct;31(10):1290-6.
23. Hamzavi I. Using light in dermatology: an update on lasers, ultraviolet phototherapy, and photodynamic therapy. *Dermatol Clin*. 2005 Apr; 23(2): 199-207
24. Hong SB, Lee MH. Topical aminolevulinic acid-photodynamic therapy for the treatment of acne vulgaris. *Photodermatol Photoimmunol Photomed*. 2005 Dec;21(6):322-5
25. Landau M. Advances in deep chemical peels. *Dermatol Nurs*. 2005 Dec;17(6):438-41.
26. Nouri K, Villafradez-Diaz LM. Light/laser therapy in the treatment of acne vulgaris. *J Cosmet Dermatol*. 2005 Dec;4(4):318-20.
27. Santos MA, Belo VG, Santos G. Effectiveness of photodynamic therapy with topical 5-aminolevulinic acid and intense pulsed light versus intense pulsed light alone in the treatment of acne vulgaris: comparative study. *Dermatol Surg*. 2005 Aug;31(8 Pt 1):910-5.
28. Uebelhoer NS, Dover JS. Photodynamic therapy for cosmetic applications. *Dermatol Ther*. 2005 May-Jun;18(3):242-52
29. Yaghami D, Garden JM, Bakus AD, Massa MC. Comparison of a 1,064 nm laser and a 1,320 nm laser for the nonablative treatment of acne scars. *Dermatol Surg*. 2005 Aug;31(8 Pt 1):903-9.
30. Charakida A, Seaton ED, Charakida M, et al. Phototherapy in the treatment of acne vulgaris: what is its role? *Am J Clin Dermatol*. 2004;5(4):211-6.
31. Briden ME. Alpha-hydroxyacid chemical peeling agents: case studies and rationale for safe and effective use. *Cutis*. 2004 Feb;73(2 Suppl):18-24.
32. Feldman S, Careccia RE, Barham KL, Hancox J. Diagnosis and treatment of acne. *Am Fam Physician*. 2004 May 1;69(9):2123-30
33. Haider, A, Shaw, JC. Treatment of acne vulgaris. *JAMA* 2004; 292:726. 30.
34. Harper JC. An update on the pathogenesis and management of acne vulgaris. *J Am Acad Dermatol*. 2004 Jul;51(1 Suppl):S36-8.
35. Omi T, Bjerring P, Sato S, et al. 420 nm intense continuous light therapy for acne. *J Cosmet Laser Ther*. 2004 Nov;6(3):156-62
36. Orringer JS, Kang S, Hamilton T, et al. Treatment of acne vulgaris with a pulsed dye laser: a randomized controlled trial. *JAMA*. 2004 Jun 16;291(23):2834-9
37. Ozolins, M, Eady, EA, Avery, AJ, et al. Comparison of five antimicrobial regimens for treatment of mild to moderate inflammatory facial acne vulgaris in the community: randomised controlled trial. *Lancet*. 2004 Dec 18-31;364(9452):2188-95
38. Pollock B, Turner D, Stringer MR, et al. Topical aminolaevulinic acid-photodynamic therapy for the treatment of acne vulgaris: a study of clinical efficacy and mechanism of action. *Br J Dermatol*. 2004 Sep;151(3):616-22.
39. Taub AF. Photodynamic therapy for the treatment of acne: a pilot study. *J Drugs Dermatol*. 2004 Nov-Dec;3(6 Suppl):S10-4. Thiboutot, D. Acne: hormonal concepts and therapy. *Clin Dermatol* 2004; 22:419
40. Tzung TY, Wu KH, Huang ML. Blue light phototherapy in the treatment of acne. *Photodermatol Photoimmunol Photomed*. 2004 Oct;20(5):266-9.
41. Jeong JT, Park JH, Kye YC. Resurfacing of pitted facial acne scars using Er:YAG laser with ablation and coagulation mode. *Aesthetic Plast Surg*. 2003 Mar-Apr;27(2):130-4.
42. Gollnick HP, Krautheim A. Topical treatment in acne: current status and future aspects. *Dermatology*. 2003;206(1):29-36

43. Seaton ED, Charakida A, Mouser PE, et al. Pulsed-dye laser treatment for inflammatory acne vulgaris: randomised controlled trial. *Lancet*. 2003 Oct 25;362(9393):1347-52
44. Kawada, A, Aragane, Y, Kameyama, H, et al. Acne phototherapy with a high-intensity, enhanced, narrow-band, blue light source: an open study and in vitro investigation. *J Dermatol Sci* 2002; 30:129.
45. Lehmann, HP, Robinson, KA, Andrews, JS, et al. Acne therapy: A methodologic review. *J Am Acad Dermatol*. 2002 Aug; 47:231-40.
46. Jordan RE, Cummins CL, Burls AJ, Seukeran DC. Laser resurfacing for facial acne scars. *Cochrane Database Syst Rev*. 2001 (1)
47. Atzori L, Brundu MA, Orru A, Biggio P. Glycolic acid peeling in the treatment of acne. *J Eur Acad Dermatol Venereol*. 1999 Mar;12(2):119-22.
48. Fulton JE, Rahimi AD. Dermabrasion using CO2 dry ice. *Dermatol Surg*. 1999 Jul;25(7):544-8.
49. Grimes PE. The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. *Dermatol Surg*. 1999 Jan;25(1):18-22.
50. US. Food and Drug Administration. Levulan Kerastick. Accessed July 2007.
51. IPLEDGE web site. Available at: <https://www.ipledgeprogram.com/>
52. United States Food and Drug Administration (FDA) 510 K Summary. CureLight's Clearlight Phototherapy Device.

Important Notice
Important Notice

General Purpose.

Health Net's National Medical Policies (the "Policies") are developed to assist Health Net in administering plan benefits and determining whether a particular procedure, drug, service or supply is medically necessary. The Policies are based upon a review of the available clinical information including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the drug or device, evidence-based guidelines of governmental bodies, and evidence-based guidelines and positions of select national health professional organizations. Coverage determinations are made on a case-by-case basis and are subject to all of the terms, conditions, limitations, and exclusions of the member's contract, including medical necessity requirements. Health Net may use the Policies to determine whether under the facts and circumstances of a particular case, the proposed procedure, drug, service or supply is medically necessary. The conclusion that a procedure, drug, service or supply is medically necessary does not constitute coverage. The member's contract defines which procedure, drug, service or supply is covered, excluded, limited, or subject to dollar caps. The policy provides for clearly written, reasonable and current criteria that have been approved by Health Net's National Medical Advisory Council (MAC). The clinical criteria and medical policies provide guidelines for determining the medical necessity criteria for specific procedures, equipment, and services. In order to be eligible, all services must be medically necessary and otherwise defined in the member's benefits contract as described in this "Important Notice" disclaimer. In all cases, final benefit determinations are based on the applicable contract language. To the extent there are any conflicts between medical policy guidelines and applicable contract language, the contract language prevails. Medical policy is not intended to override the policy that defines the member's benefits, nor is it intended to dictate to providers how to practice medicine.

Policy Effective Date and Defined Terms.

The date of posting is not the effective date of the Policy. The Policy is effective as of the date determined by Health Net. All policies are subject to applicable legal and regulatory mandates and requirements for prior notification. If there is a discrepancy between the policy effective date and legal mandates and regulatory requirements, the requirements of law and regulation shall govern. * In some states, prior notice or posting on the website is required before a policy is deemed effective. For information regarding the effective dates of Policies, contact your provider representative. The Policies do not include definitions. All terms are defined by Health Net. For information regarding the definitions of terms used in the Policies, contact your provider representative.

Policy Amendment without Notice.

Health Net reserves the right to amend the Policies without notice to providers or Members. In some states, prior notice or website posting is required before an amendment is deemed effective.

No Medical Advice.

The Policies do not constitute medical advice. Health Net does not provide or recommend treatment to members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

No Authorization or Guarantee of Coverage.

The Policies do not constitute authorization or guarantee of coverage of particular procedure, drug, service or supply. Members and providers should refer to the Member contract to determine if exclusions, limitations, and dollar caps apply to a particular procedure, drug, service or supply.

Policy Limitation: Member's Contract Controls Coverage Determinations.

Statutory Notice to Members: The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illnesses or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. The determination of coverage for a particular procedure, drug, service or supply is not based upon the Policies, but rather is subject to the facts of the individual clinical case, terms and conditions of the member's contract, and requirements of applicable laws and regulations. The contract language contains specific terms and conditions, including pre-existing conditions, limitations, exclusions, benefit maximums, eligibility, and other relevant terms and conditions of coverage. In the event the Member's contract (also known as the benefit contract, coverage document, or evidence of coverage) conflicts with the Policies, the Member's contract shall govern. The Policies do not replace or amend the Member's contract.

Policy Limitation: Legal and Regulatory Mandates and Requirements

The determinations of coverage for a particular procedure, drug, service or supply is subject to applicable legal and regulatory mandates and requirements. If there is a discrepancy between the Policies and legal mandates and regulatory requirements, the requirements of law and regulation shall govern.

Reconstructive Surgery

CA Health and Safety Code 1367.63 requires health care service plans to cover reconstructive surgery. "Reconstructive surgery" means surgery performed to correct or repair abnormal structures of the body caused by congenital defects, developmental abnormalities, trauma, infection, tumors, or disease to do either of the following:

- (1) To improve function or
- (2) To create a normal appearance, to the extent possible.

Reconstructive surgery does not mean "cosmetic surgery," which is surgery performed to alter or reshape normal structures of the body in order to improve appearance.

Requests for reconstructive surgery may be denied, if the proposed procedure offers only a minimal improvement in the appearance of the enrollee, in accordance with the standard of care as practiced by physicians specializing in reconstructive surgery.

Reconstructive Surgery after Mastectomy

California Health and Safety Code 1367.6 requires treatment for breast cancer to cover prosthetic devices or reconstructive surgery to restore and achieve symmetry for the patient incident to a mastectomy.

Coverage for prosthetic devices and reconstructive surgery shall be subject to the co-payment, or deductible and coinsurance conditions, that are applicable to the mastectomy and all other terms and conditions applicable to other benefits. "Mastectomy" means the removal of all or part of the breast for medically necessary reasons, as determined by a licensed physician and surgeon.

Policy Limitations: Medicare and Medicaid

Policies specifically developed to assist Health Net in administering Medicare or Medicaid plan benefits and determining coverage for a particular procedure, drug, service or supply for Medicare or Medicaid members shall not be construed to apply to any other Health Net plans and members. The Policies shall not be interpreted to limit the benefits afforded Medicare and Medicaid members by law and regulation.