Title: Chemical Peels

Description/Background

CHEMICAL PEELS
Chemical peels involve a controlled partial-thickness removal of the epidermis and the outer dermis. When skin is regenerated, a 2- to 3-mm band of dense, compact collagen is formed between the epidermis and the damaged layers of the dermis, resulting in ablation of fine wrinkles and a reduction in pigmentation. These changes can be long-term, lasting 15-20 years and may be permanent in some patients. Potential local complications include scarring, infection, hypopigmentation, hyperpigmentation, activation of herpes simplex, and toxic shock syndrome. (1)

Types of Peels
Chemical peels are often categorized according to the depth of the peel: categories include superficial, medium-depth, and deep chemical peels. The precise depth of the peel depends on the concentration of the agent used, duration of the application, and the number of applications. Possible indications for each type of peel and common chemicals used, as described in 2005 by Cummings et al (2) and others, is as follows:

Superficial Peels
Superficial peels (epidermal peels) affect the epidermis and the interface of the dermis-epidermis. This depth is considered appropriate for treating mild photoaging, melasma, comedonal acne, and postinflammatory erythema. Common chemical agents used for superficial peels include low concentrations of glycolic acid, 10% to 20% trichloroacetic acid (TCA), Jessner solution (a mixture of resorcinol, salicylic acid, lactic acid, and ethanol), tretinoin, and salicylic acid. As part of the treatment process, superficial peels generally cause mild erythema and desquamation, and healing time ranges from 1 to 4 days, depending on the strength of the chemical agent. With superficial peels, patients often undergo multiple sessions, generally 6 to 8 peels performed weekly or biweekly.
Medium-Depth Peels
Medium-depth peels (dermal peels) extend into the epidermis to the papillary dermis. They are used for moderate photoaging, actinic keratoses, pigmentary dyschromias, and mild acne scarring. In the past, 50% TCA was a common chemical agent for medium-depth peels, but its use has decreased due to high rates of complications (eg, pigmentary changes, scarring). Currently, the most frequently used agent is a combination of 35% TCA with Jessner solution or 70% glycolic acid. Phenol 88% alone is also used for medium-depth peels. The healing process involves mild-to-moderate edema, followed by the appearance of a new, erythematous epithelium. Patients are advised to wait at least 3 months before resuming skin care services (eg, superficial chemical peels) and repeat medium-depth chemical peels should not be performed for at least 1 year.

Deep Peels
Deep chemical peels (another type of dermal peel) penetrate the midreticular dermis and have been used for patients with severe photodamage, premalignant skin neoplasms, acne scars, and dyschromias. The most common chemical agent used is Baker solution (which consists of 3 mL of 88% phenol, 8 drops of hexachlorophene [Septisol], 3 drops of croton oil, 2 mL of distilled water). The same depth can be achieved using 50% or greater TCA peel; however, the latter has a higher risk of scarring and pigmentation problems. Phenol is cardiotoxic, and patients must be screened for cardiac arrhythmias or medications that could potentially precipitate an arrhythmia. Phenol can also have renal and hepatic toxicities.

The likelihood and potential severity of adverse events increases as the strength of the chemicals and depth of peels increases. With deep chemical peels, there is the potential for long-term pigmentary disturbances (ie, areas of hypopigmentation), and selection of patients willing to always wear makeup is advised. Moreover, chemical peels reduce melanin protection, so patients must use protective sunscreen for 9 to 12 months after a medium- to deep-facial peel.

Applications
Chemical peels are a potential treatment option for actinic keratoses and moderate-to-severe acne. Actinic keratoses are common skin lesions associated with extended exposure to the sun, with an estimated prevalence in the United States of 11% to 26%. (3) These lesions are generally considered to be a precursor of squamous cell carcinoma. (4) The risk of progression to invasive squamous cell carcinoma is unclear, but estimates vary from 0.1% to 20%. (3) For patients with multiple actinic keratoses, the risk of developing invasive squamous cell carcinoma is estimated as being between 0.15% and 80%. Treatment options include watchful waiting, medication treatment, cryosurgery, surgical resection.

Acne vulgaris is the most common skin condition among adolescents, affecting an estimated 80% of 13- to 18-year olds.(5) Acne, particularly moderate-to-severe manifestations, can cause psychologic distress including low self-esteem, depression, and anxiety. There are a variety of oral and topical treatments for acne.
Regulatory Status:

U.S. Food and Drug Administration clearance or approval of chemical agents used in peeling may not be relevant for the chemical agents used in peeling because these agents are prepared in-office, may have predated Food and Drug Administration approval, and/or may be considered cosmetic ingredients.

Medical Policy Statement

The safety and effectiveness of dermal chemical peels have been established in specific situations and may be considered a useful therapeutic option when indicated.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Note: Requests for chemical peels should be carefully evaluated to determine if the request is primarily cosmetic in nature.

Inclusions:
Chemical peels performed in a 12-month period are appropriate as follows:
• Dermal (medium and deep) chemical peels, up to four times in a 12 month period, used to treat patients with numerous (>10) actinic keratoses or other premalignant skin lesions
• Epidermal (superficial) peels, up to six times in a 12 month period, to treat active acne in patients who have failed other therapy

Exclusions:
Chemical peels are considered cosmetic when used to treat:
• Photoaged skin
• Wrinkles
• Acne scarring
• Chemical peel solutions and hydrating agents that do not require physician supervision for application

CPT/HCPCS Level II Codes (Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)

Established codes:
15788 15789 15792 15793 17360

Other codes (investigational, not medically necessary, etc.):
N/A
Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Actinic Keratoses

Clinical Context and Therapy Purpose
The purpose of dermal chemical peels for patients who have actinic keratosis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of dermal chemical peels improve the net health outcome in patients with actinic keratosis?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest are individuals with actinic keratosis.

Interventions
The therapy being considered is dermal chemical peels.

Comparators
The following therapies are currently being used to treat actinic keratosis: watchful waiting, medication treatment, cryosurgery, surgical resection, and photodynamic therapy.

Outcomes
The general outcomes of interest are destroying actinic keratosis, the durability of this effect, the development of cancerous lesions, quality of life, and the harms of associated treatment-related morbidities.
**Timing**
The relevant follow-up is within weeks for the efficacy of treatment and years for the occurrence of cancerous lesions.

**Setting**
Chemical peels are administered in an outpatient setting by dermatologists.

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of followup and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

**Systematic Reviews**
Older review articles have suggested that chemical peels might be appropriate when there are numerous lesions (ie, ≥10), making treatment of the individual lesions impractical, and when treatment constitutes a full-thickness necrosis of the epidermis, which is considered curative. (6,7)

**Nonrandomized Trials**
RCTs evaluating chemical peels for treatment of actinic keratoses were not identified. One nonrandomized split-face study was identified. Lawrence et al (1995) evaluated 15 male patients with multiple facial actinic keratoses in similar numbers on both sides of the face. (8) Patients were treated on the left side with a single application of Jessner solution plus trichloroacetic acid 35% and on the right side with fluorouracil cream 5% twice daily for 3 weeks. The efficacy of both treatments was similar. The difference in the number of actinic keratoses on the left versus right side of the face was not statistically significant at 6 or 12 months (p>0.01). Both treatments were associated with nonserious adverse events. On the chemical peel side of the face, patients developed erythema and mild desquamation lasting an average of 10 days in all but 1 patient, for whom the adverse event lasted 3 months. On the fluorouracil cream side of the face, there was erythema, scaling, erosion, and crusting; these adverse events persisted an additional 2 to 3 weeks beyond 3-week treatment period.

Kaminaka et al (2009) reported on a prospective case series from Japan that included 46 patients, 32 with actinic keratoses and 14 with Bowen disease. (9) There was no minimum number of actinic keratoses required for inclusion; ie, the study did not specifically address treatment of multiple actinic keratoses. Patients received peels with 100% pure phenol applied locally to the lesions once a month for a maximum of 8 months (or less than 8 months if a complete response was achieved sooner). Biopsies were performed on all lesions before and at the end of therapy. Twenty-nine (91%) of the 32 patients with actinic keratoses achieved a complete response (defined as an undetectable lesion at least 1 month after the last phenol application). The average number of treatments for patients with actinic keratoses was 2.9. Ten (83%) of the 12 patients with Bowen disease had a complete response, and the average number of treatments in this group was 5.5. All patients were followed for at least 1 year after treatment (median follow-up, 2.8 years). By the 1-year follow-up, 2 (4.3%) of 46 patients, one
with actinic keratoses and one with Bowen disease, had experienced recurrences. No systemic adverse events were reported. The study lacked a control group and enrolled few subjects, especially in the subset of patients with Bowen disease.

**Section Summary: Actinic Keratoses**
The evidence consists of a nonrandomized split-face study and case series. The split-face trial found similar outcomes after a single chemical peel and after 3 weeks of treatment with fluorouracil cream 5% in 15 patients. A case series found high response rates and low recurrence rates at 1 year in patients with actinic keratoses treated with phenol peels. Additional controlled studies, preferably randomized, are needed to determine the effect of chemical peels on the net health outcome in patients with actinic keratoses.

**Moderate-to-Severe Active Acne**

**Clinical Context and Therapy Purpose**
The purpose of epidermal chemical peels for patients who have moderate-to-severe active acne is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Do epidermal chemical peels improve the net health outcome in patients with moderate-to-severe active acne?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest are individuals with moderate-to-severe active acne.

**Interventions**
The therapy being considered is epidermal chemical peels.

**Comparators**
The following therapies are currently being used to treat active acne: topical or oral medications.

**Outcomes**
The general outcomes of interest are the resolution of severe acne and the harms of treatment-related morbidities.

**Timing**
The relevant follow-up is within weeks for the efficacy of treatment.

**Setting**
Chemical peels are administered in an outpatient setting by dermatologists.

**Study Selection Criteria**
Methodologically credible studies were selected using the principles outlined for indication 1.
Randomized Controlled Trials

Kaminaka et al (2014) conducted a double-blinded, placebo-controlled randomized trial using a split-face design in Japan that evaluated 26 patients with moderate-to-severe facial acne. (10) Patients with moderate acne had 6 to 20 inflammatory lesions and up to 20 noninflammatory lesions; patients with severe acne had 21 to 50 inflammatory lesions. Failure of previous treatments was not an explicit inclusion criterion. Patients had to undergo a washout period of 2 months before study participation during which they could not use topical or oral antibiotics, retinoids, or corticosteroids. Participants then received a chemical peel treatment on a randomly selected side of the face, and a placebo peel on the other side of their face. Both treatments used the same pH acid gel vehicle (pH, 2.0) and the active treatment was a glycolic acid 40% peel. Treatments were given every 2 weeks for a total of 5 applications, and follow-up occurred 2 weeks after the last session (ie, at 10-week follow-up). The overall therapeutic effect was judged by a blinded dermatologist as excellent or good for 23 (92%) of the chemical peel sides and 10 (40%) of the placebo sides; the difference between groups was statistically significant (p<0.01). Moreover, there were statistically significant reductions in inflammatory lesions, and total lesion counts at each 2-week assessment and at the final 10-week assessment. No serious side effects or systemic adverse events were reported.

Several RCTs have compared 2 types of chemical peels. (11-15) Most were conducted outside of the United States and used split-faced designs. Among the trials comparing 2 chemical peel interventions, salicylic acid was used as the chemical peel agent in all but 1 trial, which was conducted by Ilknur et al (2010) in Turkey. (12)

Dayal et al (2017) in India published a parallel-group RCT comparing salicylic acid 30% peels with peels using Jessner solution in patients with mild-to-moderate facial acne.15 Patients received six chemical peels using either solution; treatments were performed two weeks apart. At the end of the 12-week treatment period, the percent decrease in mean number of comedones was 53% in the salicylic acid group and 26% in the Jessner solution group (p=0.001). However, there was no significant difference in the decrease in mean papule counts (p=0.87) or mean pustule counts (p=0.57) at 12 weeks. The mean Michaelson Acne Severity Score, which is based on the number of comedones, papules, and pustules, was significantly better in the salicylic acid group at 12 weeks than in the Jessner solution group (p=0.002). Both treatments were generally well tolerated. Post peel burning and stinging was more common with salicylic acid and post peel erythema was more common with the Jessner solution.

An RCT by Levesque et al (2011) in France compared salicylic acid peels with peels using a lipophilic hydroxy acid derivative of salicylic acid in 20 patients. (11) To be eligible, patients had to have at least 5 noninflammatory acne lesions on each side of the face and fewer than 30 inflammatory acne lesions on the entire face. Participants were required to stop using other acne medications before starting the chemical peel treatment. In this single-blind trial, patients received 1 treatment to 1 side of their face (selected randomly) and the other treatment to the other side. Treatments occurred every other week for a total of 6 peels. At the end of the treatment period, the reduction in the proportion of noninflammatory lesions was 55.6% on the lipophilic hydroxy acid side and 48.5% on the salicylic acid side; the difference between groups was not statistically significant (p=0.88). The number of lesions decreased significantly between baseline and the end of treatment in both groups (p<0.001). Both treatments were
well tolerated (as assessed by a global tolerance scale); there was no significant difference between treatments in erythema (p=0.10).

A single-blind RCT by Ilknur et al (2010) compared glycolic acid peels with amino fruit peels. (12) The trial included 30 patients with noninflamed lesions and superficial inflamed lesions, with acne grades 0.25 to 2 using Leeds criteria. Patients received 12 peels on the 2 halves of their faces at 2-week intervals (total, 6 months). Twenty-four (80%) of 30 patients completed the trial. The mean (standard deviation) number of noninflamed lesions on the glycolic acid side decreased from 49.1 (40.6) at baseline to 18.3 (12.9) at 6 months. The mean (standard deviation) number of noninflamed lesions on the amino fruit acid side decreased from 45.6 (43.5) at baseline to 17.1 (14.2) at 6 months. The reduction in lesions did not differ significantly between groups. Findings were similar for the other primary outcome (number of superficial inflamed lesions). At 6 months, the number (standard deviation) of inflamed lesions was 6.9 (5.2) on the glycolic acid side and 7.0 (7.3) on the amino fruit acid side (p>0.05).

In 2017, Dayal et al in India published a parallel-group RCT comparing salicylic acid 30% peels to peels using Jessner solution in patients with mild-to-moderate facial acne. (15) Patients received 6 chemical peels using either solution; treatments were performed 2 weeks apart. At the end of the 12-week treatment period, the percent decrease in mean number of comedones was 53% in the salicylic acid group and 26% in the Jessner solution group (p=0.001). However, there was no significant difference in the decrease in mean papule counts (p=0.87) or mean pustule counts (p=0.57) at 12 weeks. The mean Michaelson Acne Severity Score, which is based on the number of comedones, papules, and pustules, was significantly better in the salicylic acid group at 12 weeks than in the Jessner solution group (p=0.002). Both treatments were generally well tolerated. Postpeel burning and stinging was more common with salicylic acid and postpeel erythema was more common with the Jessner solution.

Section Summary: Moderate-to-Severe Active Acne
One placebo-controlled randomized trial was identified using a split-faced design with 26 patients who had moderate-to-severe acne. Outcomes (eg, overall therapeutic effect) were significantly better in the chemical peel group. However, this trial testing a single chemical peel protocol in a relatively small number of patients provides insufficient evidence from which to draw conclusions about the safety and efficacy of chemical peels for treating active acne. Several RCTs compared 2 chemical peel agents. None of the split-faced trials found significantly better outcomes with 1 agent over the other. One parallel-group RCT had mixed findings but greater efficacy with salicylic acid peels than with Jessner solution peels for some outcomes. None of the RCTs comparing 2 chemical pool protocols included a control group that received a different treatment; therefore, it is uncertain whether either type of peel was more effective than alternative approaches to treating acne.

SUMMARY OF EVIDENCE
For individuals who have actinic keratoses who receive dermal chemical peels, the evidence includes a nonrandomized split-face study and case series. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related morbidity. The split-face study found similar outcomes after a single chemical peel or after 3 weeks of treatment with fluorouracil cream 5% in 15 patients. A case series found high response rates and low recurrence rates at 1 year in patients with actinic keratoses treated with phenol peels. Additional controlled
studies, preferably randomized, are needed. The evidence is insufficient to determine the
effects of the technology on health outcomes.

Clinical input obtained in 2010 supported the use of chemical peels for treating multiple actinic
keratoses.

For individuals who have moderate-to-severe active acne who receive epidermal chemical
peels, the evidence includes randomized controlled trials. Relevant outcomes are symptoms,
morbid events, quality of life, and treatment-related morbidity. One small randomized trial was
placebo-controlled; it found greater efficacy with active treatment than with placebo. Several
randomized controlled trials comparing chemical peel agents in patients with acne have
reported similar improvements with the types of chemical peels studied. However, no studies
were identified comparing chemical peel agents with conventional acne treatment. The
evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2010 supported the use of chemical peels as second-line treatment of
active moderate-to-severe acne.

SUPPLEMENTAL INFORMATION

Clinical Input Received through Physician Specialty Societies and Academic Medical
Centers
While the various Physician Specialty Societies and Academic Medical Centers may
collaborate with and make recommendations during this process, through the provision of
appropriate reviewers, input received does not represent an endorsement or position
statement by the Physician Specialty Societies or Academic Medical Centers, unless otherwise
noted.

In response to requests, Blue Cross Blue Shield Association received input through 3
Physician Specialty Societies and 4 Academic Medical Centers while this policy was under
review in 2010. The clinical input was consistently in agreement with the medically necessary
indications for dermal and epidermal chemical peels. Several reviewers supported use of
chemical peels for post-acne scarring.

Practice Guidelines and Position Statements

American Academy of Dermatology
The American Academy of Dermatology (2016) published guidelines on the management of
acne vulgaris, which give a B recommendation based on level II and III evidence for the use of
chemical peels for acne, with the following statement on chemical (16):

“Studies exist suggesting that chemical peels may improve acne. However, large,
multicenter, double-blinded control trials comparing peels to placebo and comparing
different peels are lacking. Glycolic acid and salicylic acid chemical peels may be
helpful for noninflammatory (comedonal) lesions. However, multiple treatments are
needed and the results are not long-lasting. In the opinion of the work group, chemical
peels may result in mild improvement in comedonal acne.”
The American Society for Dermatologic Surgery (2017) published recommendations on the use of several skin treatments following a course of isotretinoin, a treatment for severe cystic acne. (17) Previously, a number of cosmetic skin treatments, including chemical peels, were discouraged for 6 months after the use of isotretinoin. These 2017 guidelines evaluated various treatments in the context of scarring and found that superficial chemical peels were safe as a treatment either concurrent with isotretinoin or within 6 months of its discontinuation. The lack of data on medium or deep chemical peels did not permit the Society to make a recommendation on those treatments.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Ongoing and Unpublished Clinical Trials**
A search of ClinicalTrials.gov in November 2018 did not identify any ongoing or unpublished trials that would likely influence this review.

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**Government Regulations**

**National:**
National Coverage Determination (NCD) for Treatment of Actinic Keratosis (250.4), 11/26/2001

Actinic Keratosis, also known as solar keratoses, are common, sun-induced skin lesions that are confined to the epidermis and have the potential to become a skin cancer.

Various options exist for treating actinic keratosis. Clinicians should select an appropriate treatment based on the patient's medical history, the lesion's characteristics, and on the patient's preference for a specific treatment. Commonly performed treatments for actinic keratosis include cryosurgery with liquid nitrogen, topical drug therapy, and curettage. Less commonly performed treatments for actinic keratosis include dermabrasion, excision, chemical peels, laser therapy, and photodynamic therapy. An alternative approach to treating actinic keratosis is to observe the lesions over time and remove them only if they exhibit specific clinical features suggesting possible transformation to invasive squamous cell carcinoma.

Medicare covers the destruction of actinic keratoses without restrictions based on lesion or patient characteristics.

**Local:**
There is no local coverage determination.

*(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicaid Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)*
Related Policies

Ultraviolet Light Therapy Delivery Devices for Home Use (BCN only – Retired)
Photodynamic Therapy for Actinic Keratosis (Retired)

References


The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 4/9/19, the date the research was completed.
# Joint BCBSM/BCN Medical Policy History

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Next Review Date: 2<sup>nd</sup> Qtr, 2020
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: CHEMICAL PEELS

I. Coverage Determination:

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II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member’s certificate and is not guaranteed. Please consult the individual member’s certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.