Policy Statement

Electronic brachytherapy for the treatment of nonmelanoma skin cancer (see Policy Guidelines section) is considered investigational.

Policy Guidelines

Nonmelanoma skin cancer refers to squamous cell carcinoma and basal cell carcinoma. There are other less common types of skin cancer, such as T-cell lymphoma or Merkel cell tumor, which may have specific treatment options that differ from basal and squamous cell carcinomas and may need to be considered on an individual basis.

Coding

The following category III CPT code is specific for application of electronic brachytherapy to the skin surface:

- 0394T: High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed

Description

Electronic brachytherapy is a form of radiotherapy designed to deliver high-dose rate radiation to treat nonmelanoma skin cancer. This technique focuses a uniform dose of x-ray source radiation to the lesion with the aid of a shielded surface application.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Electronic brachytherapy systems for the treatment of nonmelanoma skin cancers are designed to deliver high-dose rate brachytherapy to treat skin surface lesions. This technique focuses a uniform dose of x-ray source radiation to the lesion with the aid of a shielded surface application. The Esteya® Electronic Brachytherapy System (Nucletron BV) and the Xoft® Axxent® Electronic Brachytherapy System (iCAD, Nashua, NH) are 2 systems that have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process. Food and Drug Administration product code: JAD.
Rationale

Background
Nonmelanoma Skin Cancer
Squamous cell carcinoma and basal cell carcinoma are the most common types of nonmelanoma skin cancer in the United States, affecting between 1 and 3 million people per year\(^1\,^2\) and increasing at a rate of 3\% to 8\% per year.\(^2\) Other types (e.g., T-cell lymphoma, Merkel cell tumor, basosquamous carcinoma, Kaposi sarcoma) are much less common. The primary risk factor for nonmelanoma skin cancer is sun exposure, with additional risk factors such as toxic exposures, other ionizing radiation exposure, and immunosuppression playing smaller roles.\(^2\) Although these cancers are rarely fatal, they can impact the quality of life, functional status, and physical appearance.

Treatment
Surgical
Treatment of nonmelanoma skin cancer is primarily surgical,\(^3\) and the choice of surgical procedure depends on the histologic type and size and location of the lesion. Patient preferences can also play a factor in surgical decisions due to cosmetic reasons—as well as the consideration of comorbidities and patient risk factors, such as anticoagulation. Local excisional procedures, such as electrodesiccation and curettage or cryotherapy, can be used for low-risk lesions, while surgical excision is indicated for lesions that are not low risk. Mohs surgery is an excisional procedure that uses microscopic guidance to achieve greater precision and sparing of normal tissue. In patients who meet criteria for Mohs surgery, 5-year cure rates for basal cell cancer range from 98\% to 99\%,\(^4\) making Mohs surgery the preferred procedure for those who qualify.

Radiotherapy
Radiotherapy is indicated for certain nonmelanoma skin cancers not amenable to surgery. In some cases, this is due to the location of the lesion on the eyelid, nose, or other structures that make surgery more difficult and which may be expected to have a less desirable cosmetic outcome. In other cases, surgery may be relatively contraindicated due to clinical factors, such as bleeding risk or advanced age. In elderly patients with a relatively large tumor that would require extensive excision, the benefit/risk ratio for radiotherapy may be considered favorable. The 5-year control rates for radiotherapy range from 80\% to 92\%, which is lower than that of surgical excision.\(^4\) A 1997 randomized controlled trial reported that radiotherapy for basal cell carcinoma resulted in greater numbers of persistent and recurrent lesions compared with surgical excision.\(^3\)

When radiotherapy is used for nonmelanoma skin cancer, the primary modality is external-beam radiotherapy. A number of different brachytherapy techniques have also been developed, including low-dose rate systems, iridium-based systems, and high-dose rate systems.\(^4\)

Electronic Brachytherapy
Electronic brachytherapy is a form of radiotherapy delivered locally. Available systems for treating nonmelanoma skin cancers are designed to deliver high-dose rate brachytherapy for the treatment of skin surface lesions. This technique is feasible for well-circumscribed, superficial tumors because it focuses a uniform dose of x-ray source radiation on the lesion with the aid of a shielded surface application.

A pliable mold, constructed of silicone or polymethyl-methacrylate, is fitted to the tumor surface. This mold allows treatment to be delivered to nonflat surfaces such as the nose or ear. A radioactive source is then inserted into the mold to contact the tumor and deliver a uniform radiation dosage.\(^4\)
Potential advantages of this treatment modality compared with standard radiotherapy include a shorter treatment schedule and the avoidance of radioisotopes and a dedicated treatment vault.1

Literature Review
For this evidence review, relevant outcomes will include measures of efficacy (e.g., response rates, recurrence rates) and measures of safety (e.g., skin toxicity). Cosmetic outcomes are not considered in the analysis of benefits and risks unless it is demonstrated that a poor cosmetic outcome is associated with deficits in functional status.

Electronic Brachytherapy for Nonmelanoma Skin Cancer
The available evidence on electronic brachytherapy for nonmelanoma skin cancer consists of a qualitative systematic review as well as case series. No controlled trials were identified in the published literature that compared outcomes of electronic brachytherapy with alternative treatments.

Systematic Reviews
In 2016, Delishaj et al published a systematic review of studies on high-dose rate brachytherapy, including electronic brachytherapy, for the treatment of nonmelanoma skin cancer.6 They identified 10 case series with sample sizes of 20 patients or more that reported on nonoverlapping patients. Findings were reported for 1870 patients (N=1870 lesions). The majority of lesions (65%) were basal cell carcinoma and the second largest group (35%) was squamous cell carcinoma. Reviewers did not pool study findings, reporting that the rates of local control ranged from 83% to 100%. After median follow-up ranging between 9 months to 10 years, recurrence rates ranged from 0% to 17%. Seven of the 10 studies reported recurrence rates of less than 5%, 2 had recurrence rates of 8% to 9%, and 1 study had a recurrence rate of 17%. The 2 studies with recurrence rates in the 8%-to-9% range used Leipzig applicators and the study with a 17% recurrence rate used high-dose rate brachytherapy with surface applicators or custom-made surface molds.

Case Series
We focused on uncontrolled studies that used a commercially available device for treatment, or that used a technology similar to the commercially available devices. The main characteristics and results of published case series are summarized in Table 1.

Table 1. Case Series of Electronic Brachytherapy for Nonmelanoma Skin Cancer

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Population</th>
<th>N</th>
<th>MFU, mo</th>
<th>Treatment</th>
<th>Recurrence</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paravati et al</td>
<td>Basal, squamous, or basosquamous cell</td>
<td>127</td>
<td>16.1</td>
<td>• Axxent Xoft system</td>
<td>1.2%</td>
<td>Acute:</td>
</tr>
<tr>
<td></td>
<td>carcinoma</td>
<td></td>
<td></td>
<td>• 8 fractions delivered</td>
<td>(2/154)</td>
<td>• Grade 0-1=53%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Total dose 40 Gy</td>
<td></td>
<td>• Grade 2=34.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 3=13%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Late:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 0-1=94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 2=6%</td>
</tr>
<tr>
<td>Delishaj et al</td>
<td>Nonmelanoma skin cancer</td>
<td>39</td>
<td>12</td>
<td>• Valencia applicator</td>
<td>0%</td>
<td>Acute:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 40 Gy in 8 fractions</td>
<td></td>
<td>• Grade 1=58%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 2=5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Late:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 1=19%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grade 2=2%</td>
</tr>
<tr>
<td>Tormo et al</td>
<td>Basal cell carcinoma</td>
<td>32</td>
<td>47</td>
<td>• Valencia applicator</td>
<td>3.1%</td>
<td>Grade 1=NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 42 Gy in 6-7 fractions</td>
<td></td>
<td>Grade 2=0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Grade 3=0%</td>
</tr>
<tr>
<td>Bhatnagar</td>
<td>Nonmelanoma skin cancer</td>
<td>122</td>
<td>10.0</td>
<td>• Axxent Xoft system</td>
<td>0%</td>
<td>Grade 1=11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 8 fractions delivered</td>
<td></td>
<td>Grade 2=13%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Grade 3=0%</td>
</tr>
</tbody>
</table>
The largest series was published in 2013 by Gauden et al and included 200 patients with 236 lesions (121 basal cell, 115 squamous cell). Brachytherapy was the primary treatment modality in 69% of the lesions, while in the remaining 31% (74/236) received brachytherapy as a follow-up treatment to surgery when there were positive margins. Outcomes included treatment efficacy, as measured by local recurrence rate, skin toxicity measured using Radiation Therapy Oncologic Group criteria, and cosmetic outcome using the Radiation Therapy Oncologic Group Cosmesis Scale. After a median follow-up of 66 months, there were recurrences in 2% (4/236) of treated lesions. Cosmetic outcome was judged to be excellent or good in 88% (208/236) of treated lesions. Grade 1 skin toxicity was common (71% of treated lesions); grade 2 toxicity was less common (34%); and no instances of grade 3 or higher toxicities were noted. Late hypopigmentation of treated skin was reported in 5.5% (13/236) of treated lesions.

Bhatnager (2013) published a case series using a commercially available device (Axxent eBx System; Xoft Inc., Sunnyvale, CA). The series included 122 patients with 171 nonmelanoma skin lesions. Most patients had either basal cell carcinoma (53%) or squamous cell carcinoma (41%); 10 (5.8%) patients had other types of cancer. Outcome measures included recurrence rates, adverse events using version 3.0 of the Common Terminology Criteria for Adverse Events, and cosmetic results using a standardized Cosmesis Scale. After a mean 10-month follow-up, there were no local recurrences. Dermatitis and pruritus were common early adverse events, occurring in 83% and 18% of the treated lesions, respectively. Skin hypopigmentation was the most common late adverse event, occurring in 10.9% of lesions at 1 year. Other late complications included rash (6.5%), alopecia (2.2%), and dry desquamation (2.2%). All patients had their cosmetic outcomes rated as good or excellent.

Summary of Evidence
For individuals who have nonmelanoma skin cancer who receive electronic brachytherapy, the evidence includes a systematic review and case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. No controlled trials were identified that have compared electronic brachytherapy with alternative treatment options. Further, a 2016 systematic review of case series found local control rates ranging from 83% to 100% and recurrence rates ranging from 0% to 17%. In most studies, the recurrence rate was less than 5%. In the absence of controlled studies, conclusions cannot be drawn about the efficacy and safety of electronic brachytherapy compared with other treatments for nonmelanoma skin cancer. Controlled trials are needed in defined populations that compare electronic brachytherapy with alternatives, specifically other forms of radiotherapy or surgical approaches. The evidence is insufficient to determine the effects of the technology on health outcomes.
Supplemental Information
Practice Guidelines and Position Statements

National Comprehensive Cancer Network
National Comprehensive Cancer Network guidelines on basal cell carcinoma (v.1.2017)\textsuperscript{13} and squamous cell skin cancer (v.1. 2017)\textsuperscript{14} both contain the following statement on electronic brachytherapy: “There is insufficient long-term efficacy and safety data to support the routine use of electronic brachytherapy.”

American Academy of Dermatology
Guidelines from the American Academy of Dermatology on nonmelanoma skin cancers are anticipated before the end of 2017.\textsuperscript{15}

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

Medicare National Coverage
There is no national coverage determination. In the absence of national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Ongoing Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>Xoft Electronic Brachytherapy Clinical Protocol for the Primary Treatment of Non-Melanoma Skin Cancer</td>
<td>100</td>
<td>Feb 2016 (ongoing)</td>
</tr>
<tr>
<td>NCT01016899\textsuperscript{a}</td>
<td>Electronic Skin Surface Brachytherapy for Cutaneous Basal Cell and Squamous Cell Carcinoma</td>
<td>26</td>
<td>May 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
\textsuperscript{a} Denotes industry-sponsored or cosponsored trial.

References


**Documentation for Clinical Review**

- No records required

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

IE

The following services may be considered investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>0394T</td>
<td>High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed</td>
</tr>
<tr>
<td>HCPCS</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ICD-10 Procedure</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All Diagnoses</td>
<td></td>
</tr>
</tbody>
</table>

**Policy History**

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.
8.01.62  Electronic Brachytherapy for Nonmelanoma Skin Cancer

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<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/30/2015</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
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<tr>
<td>01/01/2016</td>
<td>Coding update</td>
<td>Administrative Review</td>
</tr>
<tr>
<td>09/01/2016</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>09/01/2017</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
</tbody>
</table>

**Definitions of Decision Determinations**

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements (as applicable to your plan)**

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.