National Medical Policy

Subject: Brachytherapy for Gynecological Cancer

Policy Number: NMP454

Effective Date*: May 2009

Updated: July 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 | |

| 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
Low and High Dose Rate Brachytherapy
Health Net, Inc. considers low dose rate (LDR) and high dose rate (HDR) brachytherapy medically necessary for the treatment of uterine, cervical, endometrial and vaginal carcinoma.

Electronic Brachytherapy
Health Net, Inc. considers electronic brachytherapy investigational for gynecological cancer. Although there continues to be ongoing studies, there is still a paucity of comparative clinical trials of high dose rate electronic brachytherapy and standard brachytherapy methods, and the safety and efficacy of the high dose rate electronic brachytherapy procedure for gynecological cancer has not been determined.

Definitions
LDR  Low dose rate
HDR  High dose rate
Gy   Gray (The amount of energy absorbed in any tissue or substance from exposure, and applies to all types of radiation).
ICRU International Commission on Radiation Units
EBRT Electron beam radiation therapy
ACR  American College of Radiology
NCI  National Cancer Institute
ACS  American Cancer Society
VB   Vaginal Brachytherapy
EBT  Electronic brachytherapy

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 (may not be all inclusive)
179  Malignant neoplasm of uterus, part unspecified
180  Malignant neoplasm of cervix uteri, unspecified site
180.1 Malignant neoplasm of endocervix
180.8 Malignant neoplasm of other specified sites of cervix
182.0 Malignant neoplasm of corpus uteri, except isthmus
182.1 Malignant neoplasm of isthmus
182.8 Malignant neoplasm of other specified sites of body of uterus
183.2 Malignant neoplasm of fallopian tube
183.3 Malignant neoplasm of broad ligament of uterus
183.4 Malignant neoplasm of parametrium of uterus
183.5 Malignant neoplasm of round ligament of uterus
183.8 Malignant neoplasm of other specified sites of uterine adnexa
183.9 Malignant neoplasm of uterine adnexa, unspecified site
184.0 Malignant neoplasm of vagina
198.82 Secondary malignant neoplasm of genital organs
233.1 Carcinoma in situ of cervix uteri
233.2 Carcinoma in situ of other and unspecified parts of uterus
233.31 Carcinoma in situ, vagina

**ICD-10 Codes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>C51.0-</td>
<td>Malignant neoplasm of female genital organs</td>
</tr>
<tr>
<td>CC57.9</td>
<td></td>
</tr>
<tr>
<td>C79.82</td>
<td>Secondary malignant neoplasm of Carcinoma in situ of</td>
</tr>
<tr>
<td>D06.0-</td>
<td>Carcinoma in situ of cervix uteri</td>
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<tr>
<td>D06.9</td>
<td></td>
</tr>
<tr>
<td>D07.0-</td>
<td>Carcinoma in situ of other and unspecified genital organs</td>
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**CPT Codes**

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<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>19296</td>
<td>Placement of radiotherapy afterloading expandable catheter (single Or multichannel) into the breast for interstitial radionuclide Application following partial mastectomy, includes imaging guidance; on date separate from partial mastectomy</td>
</tr>
<tr>
<td>19297</td>
<td>Placement of radiotherapy afterloading expandable catheter (single Or multichannel) into the breast for interstitial radionuclide Application concurrent with partial mastectomy</td>
</tr>
<tr>
<td>19298</td>
<td>Placement of radiotherapy afterloading brachytherapy catheters (multiple tube and button type) into the breast for interstitial radionuclide application following (at the time of or subsequent to) partial mastectomy, includes imaging guidance</td>
</tr>
<tr>
<td>55920</td>
<td>Placement of needles or catheters into pelvic organs and/or Genitalia (except prostate) for subsequent interstitial radionuclide application</td>
</tr>
<tr>
<td>57155</td>
<td>Insertion of uterine tandems and/or vaginal ovoids for clinical Brachytherapy (Code revised in 2011)</td>
</tr>
<tr>
<td>77300</td>
<td>Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue in homogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician</td>
</tr>
<tr>
<td>77326</td>
<td>Brachytherapy isodose plan; simple (calculation made from single plane, one to four sources/ribbon application, remote afterloading brachytherapy, 1 to 8 sources) (Deleted in 2015. To report use 77316)</td>
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2015 CPT Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>77316</td>
<td>Brachytherapy isodose plan; simple (calculation[s] made from 1 to 4 sources, or remote afterloading brachytherapy, 1 channel), includes basic dosimetry calculation(s)</td>
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<tr>
<td>77317</td>
<td>Brachytherapy isodose plan; intermediate (calculation[s] made from 5 to 10 sources, or remote afterloading brachytherapy, 2-12 channels), includes basic dosimetry calculation(s)</td>
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<tr>
<td>77318</td>
<td>Brachytherapy isodose plan; complex (calculation[s] made from over 10 sources, or remote afterloading brachytherapy, over 12 channels), includes basic dosimetry calculation(s)</td>
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HCPCS Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>C1715</td>
<td>Brachytherapy needle</td>
</tr>
<tr>
<td>C1716</td>
<td>Brachytherapy source, no stranded, gold 198, per source</td>
</tr>
<tr>
<td>C1717</td>
<td>Brachytherapy seed, no stranded, high dose rate iridium 192, per source</td>
</tr>
<tr>
<td>C1719</td>
<td>Brachytherapy source, no stranded, non-high dose rate iridium 192, per source</td>
</tr>
<tr>
<td>C1728</td>
<td>Catheter, brachytherapy seed administration</td>
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<tr>
<td>C2638</td>
<td>Brachytherapy source, stranded, iodine-125, per source</td>
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<td>C2639</td>
<td>Brachytherapy source, nonstranded, iodine-125, per source</td>
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<tr>
<td>C2640</td>
<td>Brachytherapy source, stranded, palladium-103, per source</td>
</tr>
<tr>
<td>C2641</td>
<td>Brachytherapy source, nonstranded, palladium-103, per source</td>
</tr>
<tr>
<td>Q3001</td>
<td>Radioelements for brachytherapy, any type, each</td>
</tr>
</tbody>
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2015 HCPCS Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>G6003</td>
<td>Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: up to 5MeV</td>
</tr>
<tr>
<td>G6005</td>
<td>Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 11-19MeV</td>
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</table>

Brachytherapy for Gynecological Cancer Jul 15
Scientific Rationale – Update July 2015

Damast et al. (2015) completed an institutional chart review that identified 56 patients with International Federation of Gynecology and Obstetrics (FIGO) 2009 stage I-II uterine serous carcinoma (USC) treated between 2000-2010. Patients underwent total hysterectomy, bilateral salpingo-oopherectomy, and comprehensive surgical staging including pelvic and para-aortic lymph node dissection, omentectomy, and peritoneal cytology. Chemotherapy was 6 cycles of C/T, and the IVB dose was 14 Gy in 2 fractions, prescribed to 0.5 cm from the cylinder surface. Kaplan-Meier methods were used to estimate recurrence-free survival (RFS) and overall survival (OS). The median follow-up time was 49 months (range: 9-145). The 5-yr RFS and OS were 85% and 93%, respectively. In all cases of recurrence (n = 8), the first site of failure was extra-pelvic. There were no isolated vaginal recurrences, however, there was one vaginal apex recurrence recorded at 19 months in a patient with simultaneous lung metastases. Thus, the 2-year vaginal RFS was 98%. Excellent vaginal/pelvic control rates were observed. Further study of HDR brachytherapy dose and fractionation in combination with chemotherapy is worthwhile.

The NCCN Guidelines Version 2.2015 on Uterine Neoplasms and on Cervical Cancer do not mention anything about electronic brachytherapy for gynecological cancer.

In the NCCN Guidelines Version 2.2015 on Uterine Neoplasms, there was a revision under ‘Principles of Radiation therapy for Uterine Neoplasms’ which notes: “Initiate brachytherapy as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery. Brachytherapy doses for definitive therapy are individualized.” Under ‘Endometrial Cancer, Clinical Presentation; Local/regional recurrence; Therapy for Relapse’ it is noted ‘No prior RT to site of recurrence’ and ‘Previous Brachytherapy only’ pathways: “Recommendation revised as follows: “RT + Brachytherapy OR Surgical Exploration.” (Previously this was noted as and/or).

NCCN Guidelines Version 2.2015 on Uterine Neoplasms, has a section under ‘Principles of Radiation Therapy for Uterine Neoplasms’ which notes: “Tumor directed radiation therapy (RT) refers to RT directed at sites of known or suspected tumor involvement and include external beam RT (EBRT) and/or brachytherapy. Brachytherapy can be delivered to an intact uterus, either preoperative or definitively, or more commonly, to the vagina after hysterectomy. The target for vaginal brachytherapy after hysterectomy should be limited to the upper vagina.”

ACOG Practice Bulletins. Clinical Management Guidelines for Obstetricians and Gynecologists. Management of Endometrial Cancer. Number 149, April 2015. (Replaces Practice Bulletin Number 65, August 2005). This bulletin notes the following: “Vaginal brachytherapy should be the adjuvant treatment of choice over whole pelvic irradiation in certain patients with a high-intermediate risk of recurrent endometrial cancer.” (Level A recommendation - Recommendations are based on good and consistent scientific evidence).

There is a Clinical Trial on ‘Feasibility Study of the Xoft Axxent Electronic Brachytherapy System for the Treatment of Cervical Cancer’ that is currently recruiting participants. The ClinicalTrials.gov Identifier is NCT01851772 and it was last verified in January 2015. The purpose of this study is to evaluate the safety, performance and usability of the Xoft Axxent Electronic Brachytherapy System and Cervical Applicator as incorporated into the physician’s current standard treatment
practice and in replacement of high-dose-rate after-loaders using Iridium-192 or low-dose-rate Cesium treatments. Data will be collected on treatment delivery, safety, and acute toxicity. The hypothesis is that the treatment is safe as incorporated into the physician's current standard of practice. The estimated primary completion date is listed as June 2015, but it is now June 2015, and this is nowhere near completion.

**Scientific Rationale – Update July 2014**

NCCN guidelines notes that brachytherapy is a critical component of definitive therapy for all patients with primary cervical cancer who are not candidates for surgery. The guidelines do not mention the use of electronic brachytherapy.

NCCN guidelines also note that radiation therapy has been a widely used modality in the treatment of patients with endometrial cancer. The guidelines note it may included external beam radiation therapy (EBRT) and/or brachytherapy. The guidelines do not mention electronic brachytherapy.

Clinical trials are currently ongoing regarding the use of electronic brachytherapy. Zoft Inc is currently recruiting participants for a feasibility study of Axxent electronic brachytherapy system for the treatment of cervical cancer.

**Scientific Rationale – Update July 2013**

There continues to be no mention of electronic brachytherapy in the 2013 NCCN Guidelines on Cervical Cancer, nor on Uterine Neoplasms.

Brachytherapy can be delivered with either a low dose rate (LDR) or high dose rate (HDR) system. The International Commission on Radiation Units (ICRU) defines LDR as 0.4 to 2 Gy per hour, whereas HDR is delivered at >12 Gy per hour. The most common LDR sources used to treat gynecologic malignancies are Cesium-137 and Iridium-192, and the most common HDR source is Iridium-192.

There is a Clinical Trial on 'Image-Guided Gynecologic Brachytherapy (AMIGO)' that is currently recruiting participants and is sponsored by Dana Farber Cancer Institute. The ClinicalTrials.gov Identifier is NCT01399658 and it was last updated in January 2013. Standard therapy for gynecologic cancers involves the use of brachytherapy, also called internal radiation therapy or implant radiation. The treatment being studied consists of standard brachytherapy with the additional use of MRI to guide the insertion of radioactive applicators. The purpose of the study is to find out whether MRI-guided brachytherapy is practical and beneficial when compared to the standard CT-guided brachytherapy placement. The investigators are hoping that this MRI procedure will decrease the risk of giving too high a radiation dose to the bladder or bowel. The estimated primary completion date is July 2014.

The Clinical Trial on 'Feasibility Study Using the Xoft System for the Treatment of Endometrial Cancer' has recently been completed. ClinicalTrials.gov Identifier is NCT01045187 in this non-randomized study. Patients who were candidates for vaginal brachytherapy post TAH-BSO with or without EBRT were enrolled. 15 patients started and completed this study in which electronic brachytherapy was used for an FDA cleared indication. Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data.

**Scientific Rationale – Update July 2012**

National Cancer Comprehensive Network (NCCN, 2012) Recommendations:
There is no mention of electronic brachytherapy for gynecological cancer in any of the 2012 NCCN Recommendations.

National Cancer Institute (NCI, 2011):

According to the NCI, the treatment of gynecological cancers may include radioactive brachytherapy for medically inoperable women with cervical intraepithelial neoplasia or adenocarcinoma in situ and based on the size of the tumor and lymph node involvement may be a monotherapy for the treatment of stage IA cancer.

NCI also lists brachytherapy combined with EBRT as a standard treatment option for stages IA2-IVA. Radiation therapy is a treatment option for stages II-IV endometrial cancer and may include EBRT and brachytherapy.

NCI stated that vaginal cuff brachytherapy may be associated with less-radiation induced morbidity than pelvic radiation therapy. Stages I-III uterine sarcomas (e.g., carcinomsarcomes or mixed mesodermal sarcomas, leiomyosarcomas, endometrial stromal sarcomas) are typically treated surgically with adjuvant radiation therapy including brachytherapy. There is no standard treatment for patients with stage IV endometrial disease.

For vaginal cancer, brachytherapy may be a treatment option for squamous cell carcinoma in situ and stages I-IVB squamous cell and adenocarcinoma of the vagina. Brachytherapy is not discussed as a treatment option for ovarian cancer or vulvar.

There continues to be a paucity of comparative clinical trials of high dose rate electronic brachytherapy and standard brachytherapy methods. The safety and efficacy of the high dose rate electronic brachytherapy procedure for gynecological cancer has not been determined at this time.

**Scientific Rationale – Update July 2011**

McCloskey et al. (2010) retrospectively reviewed outcomes among high risk patients with endometrial cancer to determine if acceptable rates of locoregional control could be achieved with vaginal brachytherapy alone. A total of 464 patients were identified with Stage I or IIA endometrial cancer treated between January 1992 and June 2006. Of 261 patients who received post-operative RT, 225 received vaginal brachytherapy (VB) alone. Of those 225, 87 met the high risk criteria as designated by PORTEC (at least 2 of the following high risk features: age>60, Grade 3, and/or myometrial invasion >or=Occurrences of the mathematical operator' (= were changed to 'OE'. Please check.--->50%), GOG 99 (any age with 3 high risk features: Grade 2-3, >66% myometrial invasion, and/or LVSI; age >or=50 with 2 high risk features; or age >or=70 with 1 high risk feature), and/or Aalders (Stage IC, Grade 3). Descriptive recurrence statistics are provided. Among 87 high risk patients treated with VB alone, 36, 77, and 14 were high risk per PORTEC, GOG 99, and Aalders respectively. Forty (46%) underwent pelvic lymph node dissection. With a median follow-up of 52 months, 3 (3.4%) pelvic recurrences were observed including 1 vaginal recurrence, 1 pelvic recurrence, and 1 local recurrence involving both the vagina and pelvis. All 3 local recurrences were successfully salvaged with pelvic RT+/-surgery. This represents one of the largest known series of high risk localized endometrial cancer treated with VB alone. The observed 3.4% locoregional recurrence compares favorably with the 5% locoregional recurrence noted among the highest risk patients receiving pelvic RT in the PORTEC, GOG 99, and Aalders randomized trials. In this single institution experience, the 3 local recurrences were
salvaged. Based on these findings, the authors will continue to use VB alone in the adjuvant setting for patients with high risk localized endometrial cancer.

Dooley et al. (2010) completed a retrospective, multicenter study evaluated the feasibility and safety of high-dose rate electronic brachytherapy (EBT) as a postsurgical adjuvant radiation therapy for endometrial cancer. Medical records were reviewed from 41 patients (age 40-89 years) with endometrial cancer (Federation of International Gynecology and Obstetrics stages IA-IIIC) treated at nine centers between April 2008 and October 2009. Treatment included intracavitary vaginal EBT alone (n = 16) at doses of 18.0-24.0 Gy in 3-4 fractions and EBT in combination with external beam radiation therapy (EBRT, n = 25) at a total radiation dose range of 40.0-80.4 Gy. Doses were prescribed to a depth of 5 mm from the applicator surface and to the upper third (n = 15) and the upper half (n = 26) of the vagina. Median follow-up was 3.8 (range 0.5-12.0) months. All 41 patients received the intended dose of radiation as prescribed. Adverse events occurred in 13 of 41 patients and were mild to moderate (Grade 1-2), consisting primarily of vaginal mucositis, rectal mucosal irritation and discomfort, and temporary dysuria and diarrhea. There were no Grade 3 adverse events in the EBT-only treatment group. One patient, who was being treated with the combination of EBT and EBRT for recurrent endometrial cancer, had a Grade 3 adverse event. No recurrences have been reported to date. Although this study was small and retrospective, electronic brachytherapy seems promising to provide a feasible treatment option for postoperative adjuvant vaginal brachytherapy as sole radiation therapy and in combination with EBRT for primary endometrial cancer. Early and late toxicities were mild to moderate. Additional, larger clinical trials with long-term outcomes are necessary.

Dickler et al. (2010) completed a multi-center clinical study to evaluate the success of treatment delivery, safety and toxicity of EBT in patients with endometrial cancer. A modified form of high dose rate (HDR) brachytherapy has been developed called Axxent Electronic Brachytherapy (EBT). EBT uses a kilovolt X-ray source and does not require treatment in a shielded vault or a HDR afterloader unit. A total of 15 patients with stage I or II endometrial cancer were enrolled at 5 sites. Patients were treated with vaginal EBT alone or in combination with external beam radiation. The prescribed doses of EBT were successfully delivered in all 15 patients. From the first fraction through 3 months follow-up, there were 4 CTC Grade 1 adverse events and 2 CTC Grade II adverse events reported that were EBT related. The mild events reported were dysuria, vaginal dryness, mucosal atrophy, and rectal bleeding. The moderate treatment related adverse events included dysuria, and vaginal pain. No Grade III or IV adverse events were reported. The EBT system performed well and was associated with limited acute toxicities. EBT shows acute results similar to HDR brachytherapy. Additional research is needed to further assess the clinical efficacy and safety of EBT in the treatment of endometrial cancer.

The National Comprehensive Cancer Network (NCCN) 2011 Guidelines on Uterine Cancer and Cervical Cancer do not include electronic brachytherapy, in their recommendations.

There is insufficient evidence in the peer-reviewed published medical literature comparing outcomes of electronic brachytherapy with standard radioisotope-based brachytherapy at this time.

**Scientific Rationale – Update September 2010**

Electronic brachytherapy is a type of radiotherapy that utilizes a miniaturized high dose rate (HDR) X-ray source to apply radiation directly to the cancerous site. The goal is to direct the radiation dose to the size and shape of the cancerous area, sparing healthy tissue and organs.
One example of electronic brachytherapy is the Axxent Electronic Brachytherapy System (Zoft Inc.) Initially FDA approved in 2005 as substantially equivalent to devices already legally marketed in the United States, the Axxent Electronic Brachytherapy System (eBx) was initially intended to provide brachytherapy when the physician chooses to deliver intracavitary or interstitial radiation to the surgical margins following lumpectomy for breast cancer. However, in 2009, the FDA expanded the indications for use of the Axxent Balloon Applicator to deliver intracavitary or intraoperative brachytherapy wherever the physician chooses to deliver radiation treatment. On both the initial and subsequent approval, the FDA specifically noted, "The safety and effectiveness of the Axxent Electronic Brachytherapy System as a replacement for whole breast irradiation in the treatment of breast cancer has not been established."

The three components of the Axxent eBx include the Controller, Balloon Applicators-BR and X-ray Source. The Controller is a mobile platform that is responsible for the overall operation of the device. The radiation is delivered by a disposable, microminiature X-ray source located at the end of a flexible cable. The X-ray source at the distal tip of the cable is inserted into the central lumen of the appropriately-sized Balloon Applicator. The Axxent eBx System does not utilize a radioactive isotope, or require an HDR isotope afterloader, and thus does not require the heavily-shielded treatment rooms necessary for the delivery of isotope-based HDR brachytherapy.

According to the manufacturer, Zoft Inc., "The Axxent eBx System is a proprietary electronic brachytherapy platform designed to deliver isotope-free (non-radioactive) radiation treatment in virtually any clinical setting under radiation oncology supervision, without the limitations of radionuclides. Dose rates from the Axxent eBx System are set to an operating voltage of 50kV, which allows for minimal shielding, meaning the treating team can interact with the patient while delivering therapy. The Axxent System has similar dose rates to high dose rate (HDR), however, the dose fall-off rate is lower, so the patient receives less dose to critical organs and healthy tissue."

Per the manufacturer, advantages of electronic brachytherapy include, the delivery of therapeutic dose directly to the cancerous site; no radioisotope regulatory handling and safety issues; lower shielding requirements; medical personnel may remain in the room because of the unique characteristics of the system; unlike radioactive isotopes, less radiation is delivered to surrounding healthy organs and tissue and the unique design allows for multiple applications.

Peer review literature regarding HDR electronic brachytherapy is very limited and the majority of the published literature evaluates its use in the treatment of breast cancer.

Dickler et al (2010) reports a modified form of high dose rate (HDR) brachytherapy, the Axxent Electronic Brachytherapy, uses a kilovolt X-ray source and does not require treatment in a shielded vault or a HDR afterloader unit. A multi-center clinical study of 15 patients with stage I or II endometrial cancer was carried out to evaluate the success of treatment delivery, safety and toxicity of electronic brachytherapy. Patients were treated with vaginal electronic brachytherapy alone or in combination with external beam radiation. The prescribed doses of electronic brachytherapy were successfully delivered in all 15 patients. From the first fraction through 3 months follow-up, there were 4 CTC Grade 1 adverse events and 2 CTC Grade II adverse events reported that were electronic brachytherapy related. The mild events reported were dysuria, vaginal dryness, mucosal atrophy, and rectal bleeding. The moderate
treatment related adverse events included dysuria, and vaginal pain. No Grade III or IV adverse events were reported. The electronic brachytherapy system performed well and was associated with limited acute toxicities. The investigators concluded that electronic brachytherapy shows acute results similar to HDR brachytherapy. They noted, however, additional research is needed to further assess the clinical efficacy and safety of electronic brachytherapy in the treatment of endometrial cancer.

Dickler et al (2008) dosimetrically compared iridium-192 high-dose-rate brachytherapy (IB) and Xoft Axxent Electronic Brachytherapy in the treatment of endometrial cancer. The planning CT scans from 11 patients previously treated with IB were used to construct hypothetical treatment plans using the source characteristics of the XB device. The mean V95, V100, and V150 (percent of the planning target volume that received 95%, 100%, and 150% of the prescription dose) were calculated. For both the bladder and rectum, the V35 (percent of the organ that received 35% of the prescription dose) and V50 (percent of the organ that received 50% of the prescription dose) were calculated for each patient using both methods of vaginal brachytherapy. The mean %V95 was 99.7% vs. 99.6% (p = ns) and the mean %V100 was 99.0% vs. 99.1% (p = ns) for the IB and XB methods, respectively. The mean %V150 was 35.8% vs. 58.9% (p < 0.05) for the IB and XB methods, respectively. The mean bladder %V35 was 47.7% vs. 27.4% (p < 0.05) and the mean bladder %V50 was 26.5% vs. 15.9% (p < 0.05) for the IB and XB methods, respectively. The mean rectal %V35 was 48.3% vs. 28.3% (p < 0.05) and the mean rectal %V50 was 27.8% vs. 17.0% (p < 0.05) for the IB and XB methods, respectively. The investigators concluded the IB and XB methods of vaginal brachytherapy offer equivalent target volume coverage; however, the XB method allows increased sparing of the bladder and rectum.

Medicare does not have a National Coverage Determination (NCD) regarding brachytherapy. Some regions have Local Coverage Determinations (LCD’s) regarding brachytherapy noting that LDR (low dose rate) and HDR (high dose rate) brachytherapy are two delivery systems for brachytherapy, which use radioactive material to deliver a dose of intensive radiation therapy to a specific well-defined local site (treatment volume). They state in both LDR and HDR, the treatment site should be defined and accessible to the applicators that are the delivery medium for the radioactive sources.

High-dose rate (HDR) brachytherapy treatment delivery is at higher dose rates (10-100 cGy per minute). HDR is performed by using a remote afterloading device to deliver the radioactive source(s). HDR allows the dose to be delivered customarily in minutes and usually on an outpatient basis and is often given in a series of multiple fractions. HDR brachytherapy involves the use of a high activity radiation source with source radioactivity and energy far too great to allow manual handling. Local Medicare notes that HDR may be used for virtually any site in the body that is suitable for brachytherapy.

The HDR brachytherapy system uses a single, tiny (1mm by 3 mm) source that contains a highly radioactive source of Iridium-192 that is laser welded to the end of a thin, flexible stainless steel cable. The HDR machine, called a remote afterloader, safely stores the radiation source between treatments and delivers the source directly into the patient during therapy. The first step in the HDR brachytherapy process is the placement of the brachytherapy catheters, needles or other treatment applicators into the patient. Following localization radiographs or scans (simulation) and related computer based treatment planning calculations (treatment planning/dosimetry), HDR treatment is administered to the patient in a shielded vault. The computer-guided remote afterloader is used to direct the source with
millimeter precision into the applicator system. The source moves in 5mm steps to specific locations within the hollow conduits implanted in the target volume. It stops at designated positions called "dwell" positions. The distribution of radiation dose is determined by the dwell position location and how long the source remains at each of the many potential sites. HDR brachytherapy treatment courses may vary from 1 to 12 or more treatments (fractions), depending on the type of cancer being treated, the prescribed dose, whether external radiation is also being administered and many other factors.

Although the LCD’s do not specifically address electronic brachytherapy in their policies, they do list the code specific to electronic brachytherapy, 0182T (High dose rate electronic brachytherapy, per fraction) as covered for the local Medicare members that reside in the specific region when billed with one of the appropriate ICD 9 code noted in the policy (very extensive ICD 9 list).

There is insufficient evidence in the peer-reviewed literature to support the use of electronic brachytherapy for the treatment of gynecological carcinomas. Studies have been small and have not established the safety and efficacy of this treatment option. However, because electronic brachytherapy is a local Medicare covered service as dictated by the local Medicare carriers, it must be covered for all Medicare Advantage members who reside in the local area in which coverage is applicable, subject to relevant criteria and/or guidelines. For local Medicare coverage determination, please go to the individual local Medicare website.

**Scientific Rationale – Initial**

Brachytherapy is the use of radioactive isotopes to treat malignancies or benign conditions by means of a radioactive source placed close to or into the tumor or treatment site. Brachytherapy alone or combined with external beam therapy plays an important role in the management and treatment of patients with cancer. Modern brachytherapy utilizes afterloading, in which inert needles, catheters, or custom applicators are inserted before the radioactive source is advanced. A variety of applicators can be used and are selected based upon disease site, patient anatomy, and physician preference. Other treatment variables include dose-rate, mode of implantation, and whether the implant is permanent or temporary.

Brachytherapy can be delivered with either a low dose rate (LDR) or high dose rate (HDR) system. The International Commission on Radiation Units (ICRU) defines LDR as 0.4 to 2 Gy* per hour, whereas HDR is delivered at >12 Gy per hour. (*Gray [Gy] is the amount of energy absorbed in any tissue or substance from exposure, and applies to all types of radiation).

LDR brachytherapy is typically given in one to two insertions over 48 to 72 hours during an inpatient hospitalization in a shielded room. HDR is given in several fractions, most commonly three to five, for a period of several minutes per fraction, thus allowing HDR treatments to be delivered in the outpatient setting.

Consolidative or "boost" intracavitary brachytherapy allows for the delivery of high doses of radiation to the tumor while sparing the bladder and rectum due to rapid dose fall off. LDR, HDR, or pulse dose rate techniques are used, largely based upon institutional preference. For advanced presentations or disease that do not respond promptly to electron beam radiation therapy (EBRT), intracavitary techniques are often inadequate. In this case, interstitial needle brachytherapy may be required to adequately encompass gross disease.
Brachytherapy, with the development of high dose rate (HDR) systems and remote afterloaders, also allows for the precise delivery of high-dose radiation to the target tissue with sparing of the surrounding normal tissue, in a safe and efficient manner.

**Gynecological Cancer**

Brachytherapy is considered the standard of care in patients with gynecologic malignancies, specifically uterine, cervical, vaginal and endometrial tumors, and can be used to prevent local cancer recurrences after surgery or for the treatment of recurrent cancer.

Treatment for gynecological cancer will depend upon the type and the stage of cancer, involvement of surrounding tissue and structures, whether or not there is metastasis, patient’s age and comorbidities. Treatment options may include one or a combination of the following: chemotherapy, surgical intervention, hormone therapy and radiation therapy, including radioactive brachytherapy. Brachytherapy is well suited for small tumors with well-defined limits or to boost the radiation dose to the primary tumor after external beam radiation therapy (EBRT). EBRT may supplement brachytherapy to address peripheral areas such as pelvic lymph nodes.

Brachytherapy represents an integral component of treatment for gynecological cancer. One of the reasons the cure rate of these gynecologic cancers is high, compared with similar-sized cancers in other parts of the body, is that the location and growth pattern of many gynecologic cancers make them suitable for treatment with internal implantation radiotherapy.

- **Pulse Dose Rate Brachytherapy**
  - In addition to standard HDR and LDR brachytherapy, pulse dose rate brachytherapy can be utilized to treat gynecologic cancers. This technique uses a single Iridium-192 source that is programmed to move through various dwell positions in placed applicators, using remote afterloading technology. The movement of the source through the positions constitutes a single pulse, and the dose delivered per pulse, the time interval between pulses, and the total pulse duration can be varied. Pulse dose rate brachytherapy delivers a treatment in which the goal is to draw from the advantages of both HDR brachytherapy and traditional LDR brachytherapy.

While intracavitary brachytherapy is used most commonly for gynecologic malignancies, interstitial brachytherapy also may be used.

- **Intracavitary Brachytherapy** - Applicators, which will be loaded with the radioactive source, are placed inside a pre-existing body cavity, such as the vagina or uterus.
- **Interstitial Brachytherapy** - Needles are placed into the tissues at risk, such as the parametria or paravaginal tissues. The radiation source(s) are then inserted into the needles. Interstitial brachytherapy can be temporary, such as for advanced cervical cancers, or permanent, such as is the case with prostate seed implants for prostate cancer. The normal tissues of the cervix and corpus of the uterus can tolerate high doses of radiation and can recover remarkably well from radiation injury.

Brachytherapy has been used in the treatment of gynecologic tumors (uterine cervix and endometrium) employing Radium-226 (Ra-226), Cobalt-60 (Co-60), and Cesium-137 (Cs-137). The most common LDR sources used to treat gynecologic
malignancies are Cesium-137 and Iridium-192, and the most common HDR source is Iridium-192.

The American College of Radiology (ACR) has published two practice guidelines on the performance of radioactive brachytherapy. In their discussion of low dose rate (LDR), the ACR states that LDR (e.g., 226Ra, 137Cs, 192 Ir, 125I, and 103Pd) has traditionally been used to treat multiple cancers, including cervical and endometrial cancers.

In their discussions of the treatment of gynecological cancers, the National Cancer Institute (NCI, 2008) includes radioactive brachytherapy as a standard treatment option for cervical cancer stages IB–IV, endometrial stages IIB–IV, and for stage 0 vaginal squamous cell carcinoma, and stages I–IVA squamous cell and adenocarcinoma vaginal carcinomas.

**Cervical Cancer**

Brachytherapy is recommended for cervical cancer, (Stage 1B or greater) per the following professional societies:

The National Cancer Comprehensive Network (2009), the American Cancer Society (2008), the National Cancer Institute (2008), the American Society of Clinical Oncology (2007), the International Federation of Gynecology and Obstetrics (2006), and the American College of Obstetricians and Gynecology (2002).

Per the National Cancer Institute (2008), and the American Cancer Society (2008), the treatment selection for cervical cancer depends upon the stage of the disease and whether or not the carcinoma is primary or recurring. Therapy may include local or surgical excision, or total abdominal or vaginal hysterectomy, and/or conventional radiation therapy, and/or radioactive brachytherapy, and/or chemotherapy.

(2008) National Cancer Comprehensive Network (NCCN) recommends the following treatments for cervical cancer:

- For stage IB2 and IIA (>4cm), pelvic radiation therapy and concurrent cisplatinum containing chemotherapy and brachytherapy (category 1); or
- Pelvic radiation therapy and concurrent cisplatinum containing chemotherapy and brachytherapy and adjuvant hysterectomy. (category 3).

- For stage IA2, brachytherapy and pelvic radiation therapy; or
- Radical tracheectomy for fertility preservation and pelvic lymph node dissection + para-aortic lymph node sampling.

- For stage IBI and IIA (≤4cm), radical hysterectomy and pelvic lymph node dissection and para-aortic lymph node sampling (Category 2B); or
- Pelvic radiation therapy and brachytherapy; or
- Radical tracheectomy for fertility preservation and pelvic lymph node dissection + para-aortic lymph node sampling.

- For stage IB2 and IIA (>4cm), radical hysterectomy and pelvic lymph node dissection and para-aortic lymph node sampling (Category 2B); or
- Pelvic radiation therapy and concurrent cisplatinum containing chemotherapy and brachytherapy (Category 1); or
- Pelvic radiation therapy and concurrent cisplatinum containing chemotherapy and brachytherapy and adjuvant hysterectomy (Category 3).
• Adjuvant treatment for positive pelvic nodes or positive surgical margin or positive parametrium includes pelvic radiation therapy and concurrent cisplatinum containing chemotherapy (Category 1) ± vaginal brachytherapy.

(2006) In a technology assessment, the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) states that the current evidence on the safety and efficacy of high dose rate brachytherapy for carcinoma of the cervix appears adequate to support the use of this procedure, when it is administered with a curative intent.

The American College of Obstetricians and Gynecologists (ACOG) state that the following recommendation is based on good and consistent scientific evidence (Level A):

• For carcinoma of cervix stage IIB and greater should be treated with external beam and brachytherapy radiation and concurrent cisplatinum based chemotherapy

ACOG also states that both treatment strategies for carcinoma of cervix for stage Ib and early stage IIa invasive carcinoma include the following:

• Primary surgical approach with a radical hysterectomy and a pelvic lymphadenectomy, or
• Primary radiation therapy with external beam radiation and either a high dose rate or low dose rate brachytherapy.

For late stage cervical carcinoma of IIb or greater, ACOG recommends external beam radiation to achieve primary tumor reduction and provide coverage to the parametria and regional nodes at risk, supplemented by brachytherapy to increase radiation dose delivery to the central residual tumor.

The two main methods of radiation therapy (RT) delivery for cervical cancer are external photon beam RT and brachytherapy, which can be delivered using an intracavitary approach with a variety of applicators, or via an interstitial approach using needles or afterloading catheters.

For cancers of the uterine cervix, brachytherapy is usually performed after 4 to 6 weeks of external beam radiotherapy. The goal of external beam treatments is to shrink the tumor and eliminate any cancer cells that have spread to the pelvic lymph nodes. After external beam radiotherapy is completed, internal implantation for cervix cancer is most commonly done with a device called a “tandem and ovoid” applicator. These applicators consist of a hollow metal tube (the tandem) that is inserted through the cervix into the endometrial cavity. The tandem is about 10 inches long and as thin as a pencil. The ovoids are hollow metal capsules that are small enough to fit in the vagina, up against the cervix. The tandem and ovoid internal implantation procedure takes about 30 minutes. Radiation therapy is given through the tandem and ovoid applicator by placing radioactive capsules inside the hollow portions of the applicator. In most cases the applicator stays in for 40 to 48 hours.

Intracavitary brachytherapy alone is adequate treatment for stage IA1 disease. However, external beam RT is generally added to brachytherapy to improve pelvic control with more advanced disease, such as stage IB and IIA disease, both in terms of local control and overall survival. The use of external beam RT prior to brachytherapy for more advanced disease offers the following advantages:
• The decreased size of bulky endocervical tumors allows more optimal coverage by the intracavitary dose distribution, while shrinking bulky exocervical disease improves tumor geometry and therefore optimal brachytherapy placement.

• With combined therapy, the average five-year overall survival rates for women with stage IB disease are 86 to 92 percent, and for IIA disease, 75 percent.

Adjuvant radiotherapy, usually with concurrent cisplatin-based chemotherapy, offers benefit to patients with high-risk pathologic factors; these include >1/3 cervical stromal invasion, tumor diameter ≥4 cm, lymph node involvement, lymphovascular space invasion, evidence of microscopic parametrial extension, or a positive resection margin.

Definitive radiotherapy with concurrent cisplatin-based chemotherapy is a recommended treatment for patients with International Federation of Gynecology and Obstetrics (FIGO) stage IIB to IVA cervical cancer and is often preferred over surgery in earlier FIGO stage IB to IIA patients. Definitive radiation therapy may also be used for patients with early stage IA-IB1 disease, if they are not an appropriate surgical candidate, due to medical comorbidities. (Definitive radiotherapy and chemoradiotherapy include both EBRT and brachytherapy).

**Staging for cervical cancer provided by American Joint Committee on Cancer (AJCC)**

<table>
<thead>
<tr>
<th><em>TNM stage</em></th>
<th><strong>FIGO stage</strong></th>
<th>Definitions – Primary tumor (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>-</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>-</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis 0</td>
<td>I</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1 IA</td>
<td>IA</td>
<td>Cervical carcinoma confined to uterus (extension to corpus should be disregarded)</td>
</tr>
<tr>
<td>T1a IA1</td>
<td>IA1</td>
<td>Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions - even with superficial invasion - are T1b/1B. Stromal invasion with amaximal depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification</td>
</tr>
<tr>
<td>T1a2 IA2</td>
<td>IA2</td>
<td>Measured stromal invasion 3 mm or less in depth and 7 mm or less in lateral spread</td>
</tr>
<tr>
<td>T1b IB</td>
<td>IB</td>
<td>Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2</td>
</tr>
<tr>
<td>T1b1 IB1</td>
<td>IB1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b2 IB2</td>
<td>IB2</td>
<td>Clinically visible lesion more than 4.0 cm</td>
</tr>
<tr>
<td>T2 II</td>
<td>II</td>
<td>Cervical carcinoma invades beyond uterus but not to pelvic wall or to the lower third of vagina</td>
</tr>
<tr>
<td>T2a IIA</td>
<td>IIA</td>
<td>Tumor without parametrial invasion</td>
</tr>
<tr>
<td>T2b IIB</td>
<td>IIB</td>
<td>Tumor with parametrial invasion</td>
</tr>
<tr>
<td>T3 III</td>
<td>III</td>
<td>Tumor extends to the pelvic wall, and/or involves the lower third of the vagina, and/or causes hydronephrosis or nonfunctioning kidney</td>
</tr>
<tr>
<td>T3a IIIA</td>
<td>IIIA</td>
<td>Tumor involves lower third of the vagina, no extension to pelvic wall</td>
</tr>
<tr>
<td>T3b IIIB</td>
<td>IIIB</td>
<td>Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney</td>
</tr>
</tbody>
</table>
| IV          |                | Cervical carcinoma has extended beyond the true pelvis or has
involved (biopsy proven) the bladder mucosa or rectal mucosa. 
Bullous edema does not qualify as a criterion for stage IV disease.

T4 IVA Spread to adjacent organs (bladder, rectum, or both) 
M1 IVB Distant metastasis

*TNM – Tumor, Node, Metastasis 
**FIGO - International Federation of Gynecology and Obstetrics

**Endometrial Cancer**

Brachytherapy is recommended for endometrial cancer (Stage IIB and greater) by the following professional organizations:

The National Cancer Comprehensive Network (2009), the National Cancer Institute (2008), the American Cancer Society (2008), and the International Federation of Gynecology and Obstetrics (2006).

Endometrial carcinoma is primarily a surgically managed disease. Due to the presence of early symptoms, most commonly vaginal bleeding, the majority of women with endometrial carcinoma are diagnosed with uterine-confined disease. The need for adjuvant postoperative therapy is governed by the pathologic findings at the time of surgery.

Per the National Cancer Institute (2008), the American Cancer Society (2008) and the Federation of Gynecology and Obstetrics (FIGO), the standard surgical treatment involves total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal washings, and assessment of the pelvic and para-aortic nodes. If the cancer is more extensive, preoperative and/or adjunctive intracavitary and external conventional radiotherapy, and/or vaginal radioactive brachytherapy and/or hormonal therapy, and/or chemotherapy may be indicated. Vaginal radioactive brachytherapy is also indicated for the treatment of vaginal cuff involvement.

In the treatment of endometrial cancer, the American Cancer Society (ACS, 2008) states that low-dose or high-dose radioactive brachytherapy may be used.

(2009) National Comprehensive Cancer Network (NCCN)
Given that vaginal brachytherapy is associated with significantly less toxicity than pelvic radiation therapy, it has been suggested that vaginal brachytherapy alone is a reasonable choice for most patients with uterine-confined endometrial cancer who are deemed candidates for adjuvant radiotherapy. A recent pooled randomized trial (ASTEC/EN.5) found that adjuvant pelvic radiation therapy alone did not improve survival in patients with intermediate-risk or high-risk early-stage endometrial cancer. Soderini et al. (2003), Keys et al. (2004) and Creutzberg et al. (2000) completed a meta-analysis of 5 randomized trials that found that adjuvant pelvic radiation therapy for stage I disease was associated with a slight survival advantage in high-risk patients but not in lower risk patients. The relative applications of brachytherapy and/or whole pelvic radiation therapy should be carefully tailored to a patient’s pathologic findings.

(2009) National Comprehensive Cancer Network (NCCN) states that brachytherapy doses for definitive therapy are individualized based on the clinical situation. For postoperative therapy in patients with endometrial gross IIB disease, in general, a total dose of 78-80 Gy low dose rate equivalent to the tumor volume is recommended. For vaginal brachytherapy the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT.
EN.5 and ASTEC were set up as individual trials to investigate the benefit or otherwise of postoperative adjuvant pelvic radiotherapy in women with early endometrial cancer and pathological features suggestive of intermediate or high risk of recurrence and death. The EN.5 trial of the National Cancer Institute of Canada (NCIC) Clinical Trials Group started in 1996, but could not recruit sufficient patient numbers to complete the study as it was originally envisaged. In 1998, the UK Medical Research Council (MRC) launched ASTEC, and invited the NCIC Clinical Trials Group to plan a prospective combination of the EN.5 data with those of ASTEC. ASTEC/EN.5 therefore consists of two trials with separate randomisations combined to make one intergroup trial. This trial was completed in 2009 as noted above.

(2009) There is currently an ongoing Clinical Trial, which stated in 2006, on ‘External-Beam Radiation Therapy or Implant Radiation Therapy Compared With Observation in Treating Patients Who Have Undergone Surgery for Stage I Endometrial Cancer.’ This randomized phase III trial is known as the ‘Portec 2 Study.’ It is studying external-beam radiation therapy or brachytherapy known as implant radiation therapy to see how well they work compared with observation in treating patients who have undergone surgery for stage I endometrial cancer.

When radiotherapy is given for patients with endometrial cancer, it is usually given after a hysterectomy. Radiotherapy is usually given with both external beam irradiation and internal implantation, or brachytherapy. Most patients receive three separate internal implantation treatments, separated by a week. The goal of internal implantation in this setting is to deliver a boost dose of radiation to the tissues near the upper part of the vagina. An applicator is fitted to the vagina, and high-dose-rate brachytherapy is given via the applicator. Radiation treatments are completed in about 15 minutes. The entire internal implantation session takes about 45 minutes.

The American Brachytherapy Society has published its recommendations for HDR brachytherapy in the management of endometrial carcinoma. One of the more common dose fractionation schedules employed is three, once-weekly fractions of 7 Gy each, delivered to a depth of 5 mm from the vaginal mucosal surface.

### Stages of Endometrial Cancer

Endometrial carcinoma is surgically staged according to the joint International Federation of Gynecology and Obstetrics (FIGO)/American Joint Committee on Cancer (AJCC) classification system.

<table>
<thead>
<tr>
<th>TNM categories</th>
<th>FIGO stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td></td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>Tumor confined to corpus uteri</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumor limited to endometrium</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumor invades up to or less than one-half of the myometrium</td>
</tr>
<tr>
<td>T1c</td>
<td>IC</td>
<td>Tumor invades to more than one-half of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor invades cervix but does not extend beyond uterus</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Endocervical glandular involvement only</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Cervical stromal invasion</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Local and/or regional spread as specified in T3a, b, and/or N1 and FIGO IIIA, B, and C below</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumor involves uterine serosa and/or adnexa (direct</td>
</tr>
</tbody>
</table>
extension or metastasis) [often termed stage IIIA2] and/or cancer cells in ascites or peritoneal washings [stage IIIA1]

<table>
<thead>
<tr>
<th>T3b</th>
<th>IIIB</th>
<th>Vaginal involvement (direct extension or metastasis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>IIIC</td>
<td>Metastasis to the pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumor invades bladder mucosa and/or bowel mucosa (Bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
<td>Distant metastasis. (Excluding metastasis to vagina, pelvic serosa, or adnexa. Including metastasis to intra-abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes)</td>
</tr>
</tbody>
</table>

Postsurgical management of endometrial carcinoma depends on the estimate of the likelihood of disease recurrence. Women in the following risk factors meet all of criteria noted:

**Low-risk:**

- Grade 1 or 2 histology
- Invasion limited to the endometrium (stage IA) or invasion through less than one-half of the myometrium (stage IB)

We recommend TAH-BSO alone for women with low-risk endometrial cancer (Grade 1B).

**Intermediate-risk:**

- **Grade 1 or 2** tumor extending beyond one-half of the myometrium (stage IC), or
- **Grade 3** tumor with invasion limited to the endometrium (stage IA) or invasion through less than one-half of the myometrium (stage IB).

**High-risk:** (Considered to be at high risk for disease persistence or recurrence)

- **Grade 3 cancer** with invasion of more than one-half of the myometrium (stage IC, grade 3), or
- **Stage IIA or greater disease**, regardless of grade, although the prognostic significance of involvement of the endocervical glands only (i.e., stage IIA disease), independent of other high-risk features, is not well characterized.
- Patients with lymphovascular space or lower uterine segment involvement, and papillary serous or clear cell histology are also at an elevated risk for metastatic, persistent, and recurrent disease

(2002) Per the American College of Obstetricians and Gynecology (ACOG):
The following recommendations are based on good and consistent scientific evidence (Level A):

- For stage Ib and selected IIA carcinomas of the cervix, either radical hysterectomy and lymph node dissection or radiation therapy with cisplatin-based chemotherapy should be considered. Adjuvant radiation therapy may be required in those treated surgically, based on pathologic risk factors, especially in those with stage Ib2 carcinoma.
Stage IIb and greater should be treated with external-beam and brachytherapy radiation and concurrent cisplatin-based chemotherapy.

**Vaginal Cancer**

Brachytherapy is recommended for vaginal cancer (Stage 1 and greater) by the following professional organizations:

- The National Cancer Institute (2008),
- the American Cancer Society (2008),

Radiotherapy for vaginal cancer is usually given with a combination of external beam irradiation and internal implantation radiotherapy. Unlike the technique of internal implantation described in the above section on endometrial cancer, internal implantation for vaginal cancer is usually done under anesthesia. Usually, plastic needles are inserted into the tissues involved with cancer. Radiation therapy is given by placing radioactive wires inside the plastic needles. After the implantation procedure the patient is isolated for about 48 hours with the implant and radioactive wires in position.

Vaginal brachytherapy demonstrated clearly reduced toxicity, specifically of diarrhea, than pelvic EBRT. Quality of life analysis suggested that brachytherapy was associated with better social functioning and fewer limitations in daily activity as a result of bowel problems than pelvic EBRT.

- Adjuvant vaginal cuff brachytherapy — Approximately 75 percent of recurrences in patients with stage I, uterine-confined disease, are located at the vaginal apex, and vaginal cuff brachytherapy is very effective in reducing this risk of local recurrence.

- Vaginal cuff brachytherapy is typically accomplished using HDR therapy with an Iridium-192 source, but also can be delivered using LDR therapy. Treatment is initiated three to six weeks following surgery and consists of three to five fractions given once or twice weekly on an outpatient basis. In general, the upper one-half to upper two-thirds of the vagina is treated and both vaginal ovoids or a vaginal cylinder can be used as applicators for vaginal cuff brachytherapy. The prescription dose depends upon the number of fractions and dose specification point (to the vaginal mucosa or to a depth of 5 mm), and several published fractionation schedules are accepted.

**Vaginal Cancer**

Per the International Federation of Gynecology and Obstetrics (FIGO), the treatment options for vaginal cancer include the following:

- Radiation therapy (EBRT in combination with radioactive brachytherapy) is the treatment of choice for most cases.
- Stage I and stage II (select cases) - intracavitary radioactive brachytherapy
- Larger lesions - EBRT in combination with radioactive brachytherapy
- Vaginal intraepithelial neoplasia - radioactive brachytherapy

**The Stages of Vaginal Carcinoma are noted below:**

- Stage 0 - carcinoma in situ; intraepithelial neoplasia grade 3
- Stage I - carcinoma is limited to the vaginal wall
- Stage II - carcinoma has involved the subvaginal tissue but has not extended to the pelvic wall
- Stage III - carcinoma has extended to the pelvic wall
- Stage IV - carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum; bullous edema as such does not permit a case to be allotted to stage IV
- Stage IVA - tumor invades bladder an/or rectal mucosa and/or direct extension beyond the true pelvis
- Stage IVB - spread to distant organs

**Uterine Carcinoma**

Uterine sarcomas are rare malignancies with a poor prognosis, diagnosed in less than 3% of gynecological carcinomas. There are several types of uterine sarcomas including endometrial stromal, rhabdomyosarcoma, leiomyosarcoma, high-grade undifferentiated. Symptoms may include abnormal vaginal bleeding or discharge and pelvic pain. Diagnostic workup typically includes endometrial sampling. If the biopsy is inconclusive, a hysteroscopy or dilation and curettage may be performed. Chest radiography, CT scan of the thorax or pelvis, MRI of the pelvis, and other diagnostic studies may be indicated to determine if metastases has occurred. Per the National Comprehensive Cancer Network (2008), and the American Cancer Society (2008), standard treatment involves surgical intervention and proposed adjuvant therapies (e.g., hormone therapy, chemotherapy, radiotherapy with or without radioactive brachytherapy) may be indicated.

**Electronic Brachytherapy**

Electronic brachytherapy has been developed to offer advantages over standard radioactive brachytherapy in the areas of radiation safety both to the patient as well as the personnel administering the treatment. The Axxent Electronic Brachytherapy System uses disposable miniature X-ray radiation sources to deliver electronically generated ionizing radiation directly to tumor beds. Electronic brachytherapy is intended to minimize exposure of the patient's healthy tissue to unnecessary radiation. Electronic brachytherapy uses X-ray energy to allow more flexibility than radioisotope-based brachytherapy systems that are currently in use. Electronic brachytherapy does not require a heavily shielded environment, so that it has potential for use in a broad array of clinical settings.

Electronic brachytherapy has potential for use in administering high-dose rate brachytherapy for breast cancer (California Technology Assessment Forum [CTAF], 2006). However, there is insufficient evidence in the peer-reviewed published medical literature comparing outcomes of electronic brachytherapy with standard radioisotope-based brachytherapy.

Therefore, in summary, due to the paucity of comparative clinical trials of high dose rate electronic brachytherapy and standard brachytherapy methods, the safety and efficacy of the high dose rate electronic brachytherapy procedure has not been determined. The professional organizations, such as the National Cancer Institute (NCI), the American Cancer Society (ACS) and the American College of Radiology (ACR), all promote brachytherapy for endometrial cancer, not electronic brachytherapy.

The American College of Radiation Oncology (ACRO) posted an alert stating that "There are currently no regulations or training requirements" for the use of electronic brachytherapy, and guidelines will be forthcoming from the Conference of Radiation Control Program Directors (CRCPD) (ACRO, 2008; Holt et al, 2008). As of the present time, 2009, there are neither guidelines to regulate the use of electronic brachytherapy nor training requirements.
Summary
Evidence in the peer-reviewed scientific literature as well as professional societies and organizations support the safety and efficacy of the use of radioactive brachytherapy for the treatment of cervical, endometrial, uterine and vaginal carcinomas. Radioactive brachytherapy is typically used in conjunction with external beam conventional radiation therapy, but it may be used as a primary monotherapy or adjunctive monotherapy. It may also be used concurrently with chemotherapy.

Review History
May 2009 Medical Advisory Council Initial Approval
September 2010 Added Medicare table and link to Local Coverage Determinations for brachytherapy. Code updates.
July 2011 Update. Added revised Medicare Table with link to LCD. Updated Codes. No revisions.
July 2012 Update. No revisions.
July 2013 Update. No revisions. Codes updated.
July 2014 Update – no revisions

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

References – Update July 2015
References – Update July 2014

References – Update July 2013

References – Update July 2012
References- Update July 2011

References- Update September 2010

References Initial

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
Brachytherapy for Gynecological Cancer

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 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 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 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.