



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Brachytherapy for Gynecological Cancers

Effective Date 11/15/2010
Next Review Date.....11/15/2011
Coverage Policy Number 0483

Table of Contents

Coverage Policy	1
General Background	1
Coding/Billing Information	4
References	5
Policy History.....	11

Hyperlink to Related Coverage Policies

Cervical Cancer Screening Technologies
 Endometrial Ablation
 Hysterectomy
 Inpatient Admission for Radiation Therapy
 Intraoperative Radiation Therapy
 Transvaginal Ultrasound for Ovarian and Endometrial Cancer Screening or Surveillance
 Uterine Artery Embolization

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers radioactive brachytherapy as medically necessary for the treatment of cervical, endometrial, uterine and vaginal carcinoma.

CIGNA does not cover electronic/kilovoltage brachytherapy for the treatment of gynecological cancers because it is considered experimental, investigational or unproven.

General Background

Gynecological cancer is defined as cancers that involve the female reproductive system, including the cervix, endometrium, fallopian tubes, ovaries, uterus, vagina, and vulvar. Treatment for gynecological cancer will depend on the type of cancer, the stage of the cancer, involvement of surrounding tissue and structures, whether or not there is metastasis, and patient's age and comorbidities. Treatment options may include one or a combination of the following: chemotherapy, surgical intervention, hormone therapy, external beam radiation therapy, and/or radioactive brachytherapy.

Radioactive brachytherapy is a type of radiation therapy that involves the placement of sealed sources of radioactive materials (e.g., cesium-137, cobalt-60, gold-198, iodine-125, palladium-103) into body tissue or into

a body cavity. Interstitial and intracavitary brachytherapy are the most commonly used forms of radioactive brachytherapy for the treatment of gynecological carcinomas. Interstitial radioactive brachytherapy involves placing radioactive materials (e.g., seeds, pellets) into the tissue using needles or small diameter catheters. Intracavitary radioactive brachytherapy indicates implantation of radioactive materials via an applicator into a body cavity (e.g., tandem inserted into the uterus, ovid inserted into the vaginal vault). The implanted radiation is emitted outward from a radioactive isotope to treat surrounding areas. The dosage of radioactive brachytherapy depends upon the rate at which it is delivered (i.e., low-dose rate [LDR]) or high-dose rate [HDR]). Proponents of radioactive brachytherapy state that, due to the rapid falloff of dose away from the source, radioactive brachytherapy provides maximal radiation dose escalation, resulting in more effective local tumor control, and confinement of radiation to the tumor region, sparing healthy tissue (National Cancer Institute [NCI], 2010a; Bradley and Petereit, 2006; Li, 2006; Patel and Arthur, 2006; Shakespeare, et al., 2006; Ferrigno, et al., 2005). Radioactive brachytherapy is an established treatment option for cervical, endometrial, uterine and vaginal carcinomas. However, due to insufficient evidence, radioactive brachytherapy is not an established therapy for fallopian, ovarian or vulvar cancers.

As an alternative to radioactive brachytherapy, electronic brachytherapy has been proposed for the treatment of gynecological carcinomas. Electronic brachytherapy (eBx) uses a 50 kilovoltage x-ray approach and is proposed to deliver HDR by mimicking the penetration and dosage characteristics of radioactive Iridium-192. For the treatment of endometrial cancer, eBx is used to deliver radiation by the insertion of a vaginal cylindrical applicator. In addition to not having to use radioactive material, other proposed advantages of eBx compared to radioactive HDR include the delivery of radiation at a lower energy, a sharper dose-fall off, and greater protection to surrounding tissue (Dickler, et al., 2008; U.S. Food and Drug Administration, May 2008; Xoft, 2009). There are a limited number of studies comparing the use of eBx to radioactive brachytherapy or to other conventional treatments. The data in the published peer-reviewed scientific literature are insufficient to support the use of eBx for the treatment of gynecological carcinomas (Holt and Rivard, 2008).

U.S. Food and Drug Administration (FDA)

The FDA approves a radionuclide brachytherapy source as a 510(k) Class II therapeutic, radiology device “that consists of a radionuclide which may be enclosed in a sealed container made of gold, titanium, stainless steel, or platinum and intended for medical purposes to be placed onto a body surface or into a body cavity or tissue as a source of nuclear radiation for therapy” (FDA, 2009). An example of a radionuclide device is the SPEC Model M-19 Iridium-192 brachytherapy source (Source Production & Equipment Co., Inc., St. Rose, LA) (FDA, 2006).

The Axxent[®] Electronic Brachytherapy System (Xoft, Inc., Fremont, CA) was approved by the 510(k) process for “use with the Axxent Applicators to treat lesions, tumors and conditions in or on the body where radiation is indicated” (FDA, Feb 2008). The Axxent[®] Vaginal Applicator Set was approved by the FDA “to deliver high dose rate X-ray radiation for brachytherapy” (FDA, May 2008; FDA, Feb 2008).

Literature Review - Radioactive Brachytherapy

Cervical Carcinoma: Evidence in the published peer-reviewed scientific literature in the form of systematic reviews (Wang, et al., 2010; Viani, et al., 2009; Stewart and Viswanathan, 2006), randomized controlled trials (Lertsanguansinchai, et al., 2004; Nam and Ahn, 2004; Tanake, et al., 2003; Hareyama, et al., 2002), prospective case series (Vrdoljak, et al., 2006; Shakespeare, et al., 2006; Chung, et al., 2005), and retrospective reviews (Ferrigno, et al., 2005; Park, et al., 2002; Kim, et al., 2001) support the use of radioactive brachytherapy for the treatment of cervical carcinoma.

In a technology assessment, the National Institute for Health and Clinical Excellence (NICE) (2006) (United Kingdom) stated 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.

Endometrial Carcinoma: Brachytherapy for the treatment of endometrial carcinoma is supported by outcomes in randomized controlled trials (Nout, et al., 2009; Sorbe, et al., 2009; Sorbe, et al., 2005), comparative studies (Cengiz, et al., 2005), prospective case series (Alektiar, et al., 2005; Fanning, 2001), and retrospective reviews (Lin, et al., 2007; Rossi, et al., 2007; Jolly et al., 2005).

Uterine Carcinoma: Although the evidence supporting radioactive brachytherapy for uterine cancer is primarily in the form of retrospective reviews (Livi, et al., 2003), radioactive brachytherapy is considered an accepted treatment option for this patient population.

Vaginal Carcinoma: Evidence in the form of randomized controlled trials and retrospective reviews (Nout, et al., 2010; Ogino, et al., 2001; Xiang-E, et al., 1998) supports radioactive brachytherapy for the treatment of vaginal cancer. Although the evidence is limited, radioactive brachytherapy is considered an established treatment option for vaginal carcinoma.

Other Gynecological Carcinomas: Radioactive brachytherapy is not an established treatment option for fallopian, ovarian or vulvar carcinomas. There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and efficacy of radioactive brachytherapy for these gynecological carcinomas.

Clinical trials have been conducted to investigate the use of intraperitoneal radioactive chromic phosphate (^{32}P) for the treatment of ovarian cancer. Young et al. (2003) conducted a randomized controlled trial (RCT) and compared the outcomes of intraperitoneal ^{32}P (n=110) to cyclophosphamide-cisplatin (CP) (n=119) in women with FIGO stages IA-II ovarian cancer. The ten-year cumulative incidence of recurrence for ^{32}P patients was 35% (95% CI, 27% to 45%) compared to 28% (95% CI, 21% to 38%) for the CP patients. CP patients experienced a recurrence rate that was 29% lower than the ^{32}P patients, and the death rate was 17% lower for the CP patients (not statistically significant). A lower rate of complications was reported for the CP patients. Varia et al. (2003) compared the outcomes of 202 ovarian cancer patients treated with radioactive ^{32}P compared to no additional therapy. With a median follow-up of 63 months in surviving patients, 68 ^{32}P patients and 63 no therapy patients developed tumor recurrence. There was no significant difference in overall survival between the two groups (p=0.19). Dent et al. (2000) also conducted an RCT in which 287 patients with ovarian cancer were randomized to whole abdominal radiotherapy (RT) or melphalan or radioactive intraperitone ^{32}P . Overall survival estimates at 10 years were 45% in the RT Group; 49% in the melphalan group, and 50% in the ^{32}P group (p=0.30). Relapse-free survival estimates at 10 years included 50% in the RT group, 62% in the melphalan group, and 51% in the ^{32}P group (p=0.147). There were no significant differences in the overall or disease-free survival rates between the groups.

There is insufficient evidence to support the use of radioactive brachytherapy for the treatment of vulvar cancer. Evidence evaluating this use is limited and primarily in the form of small case series (n=9) (Seegar, et al., 2006) and retrospective reviews (n=11) (Tewari, et al., 1999).

Literature Review - Electronic Brachytherapy (eBx)

There is insufficient evidence in the published peer-reviewed scientific literature to support electronic brachytherapy for the treatment of gynecological carcinomas. Studies are primarily in the form of small (n=11–15) case series and retrospective reviews with short-term follow-up (e.g., three months) for the treatment of endometrial cancer (Dickler, et al., 2010; Dickler, et al., 2008) and have not established the safety and efficacy of this treatment option.

Professional Societies/Organizations

American Cancer Society (ACS): The ACS states that radioactive brachytherapy may be a treatment option for cervical (ACS, 2010a), endometrial (ACS, 2010b), and vaginal cancers (ACS, 2010c), but is rarely used for the treatment of ovarian cancers (ACS, 2010d). As it relates to uterine sarcoma, the ACS states that low dose or high dose brachytherapy may be used (ACS, 2010e).

American College of Obstetricians and Gynecologists (ACOG): In their 2005 guidelines on the management of endometrial cancer, ACOG listed vaginal brachytherapy as an adjuvant radiation treatment option. Based on “good and consistent scientific evidence”, ACOG (2002) stated that stage IIB or greater cervical carcinoma should be treated with external beam radiation therapy (EBRT), HDR or LDR brachytherapy, and chemotherapy.

American College of Radiology (ACR): The ACR published two practice guidelines on the performance of radioactive brachytherapy. In their discussion of low-dose rate (LDR) brachytherapy, the ACR states that LDR (e.g., radium-226, cesium 137, iodine-125, and palladium-103) has traditionally been used to treat multiple cancers, including cervical and endometrial (ACR, 2010a). The ACR states that “HDR is indicated for the treatment of malignancies where the treatment site can be well defined and accessible to applicators to hold the sources”. It is used for cervical, endometrial and vaginal cancers (ACR, 2010b).

International Federation of Gynecology and Obstetrics (FIGO): The 2006 FIGO guidelines discussed the screening, diagnosis and management of gynecological cancers. According to FIGO, radioactive brachytherapy is a treatment option for cervical, endometrial and vaginal carcinomas. Brachytherapy may be used in combination with EBRT and/or chemotherapy and in some cases as a monotherapy (e.g., poor surgical candidates, vaginal intraepithelial neoplasia). Regarding vulvar carcinoma, FIGO states that “in some cases, the positive margin may be boosted with brachytherapy”, but that the technique requires experience to avoid the excessive risk of necrosis.

National Cancer Institute (NCI): According to the NCI, the treatment of gynecological cancers may include radioactive brachytherapy as a standard treatment option for cervical cancer (NCI, 2010a), endometrial cancer (NCI, 2010b), squamous cell carcinoma, and adenocarcinoma vaginal carcinomas (NCI, 2010c).

National Comprehensive Cancer Network® (NCCN®): In their oncology practice guidelines, NCCN (2010a) discusses the use of radioactive brachytherapy as an adjuvant treatment option for patients with cervical cancer. It may be used in conjunction with radiotherapy and, in some cases, concurrent chemotherapy. For the treatment of uterine neoplasms, NCCN (2010b) states that radioactive brachytherapy may be the primary treatment option or an adjuvant therapy for endometrial carcinomas and extrauterine disease (i.e., vaginal, bladder, bowel/rectum, parametrial). It may also be used for inoperable carcinoma limited to the uterus and as a salvage therapy.

Summary

Evidence in the published 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.

There is insufficient evidence in the published peer-reviewed scientific literature to support electronic/kilovoltage brachytherapy for the treatment of gynecological cancers. Larger, well-designed studies are needed to establish the safety and efficacy of this treatment modality.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
55920	Placement of needles or catheters into pelvic organs and/or genitalia (except prostate) for subsequent interstitial radioelement application
57155	Insertion of uterine tandems and/or vaginal ovoids for clinical brachytherapy
58346	Insertion of Heyman capsules for clinical brachytherapy
77326	Brachytherapy isodose plan; simple (calculation made from single plane, one to four sources/ribbon application, remote afterloading brachytherapy, 1 to 8 sources)
77327	Brachytherapy isodose plan; intermediate (multiplane dosage calculations, application involving 5 to 10 sources/ribbons, remote afterloading brachytherapy, 9 to 12 sources)
77328	Brachytherapy isodose plan; complex (multiplane isodose plan, volume implant calculations, over 10 sources/ribbons used, special spatial reconstruction, remote afterloading brachytherapy, over 12 sources)
77761	Intracavitary radiation source application; simple
77762	Intracavitary radiation source application; intermediate
77763	Intracavitary radiation source application; complex

77776	Interstitial radiation source application; simple
77777	Interstitial radiation source application; intermediate
77778	Interstitial radiation source application; complex
77785	Remote afterloading high dose rate radionuclide brachytherapy 1 channel
77786	Remote afterloading high dose rate radionuclide brachytherapy; 2-12 channels
77787	Remote afterloading high dose rate radionuclide brachytherapy; over 12 channels
77790	Supervision, handling, loading of radiation source

HCPCS Codes	Description
S2270	Insertion of vaginal cylinder for application of radiation source or clinical brachytherapy (report separately in addition to radiation source delivery)

ICD-9-CM Diagnosis Codes	Description
179	Malignant neoplasm of uterus, part unspecified
180.0	Malignant neoplasm of endocervix
180.1	Malignant neoplasm of exocervix
180.8	Malignant neoplasm of other specified sites of cervix
180.9	Malignant neoplasm of cervix uteri, unspecified site
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
183.3	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
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

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
0182T	High dose rate electronic brachytherapy, per fraction

*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	11/15/2007	0483	Brachytherapy for Gynecological Cancers

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