



# 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 Prostate Cancer**

**Effective Date ..... 12/15/2010**  
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**Coverage Policy Number ..... 0419**

## Table of Contents

Coverage Policy .....	1
General Background .....	1
Coding/Billing Information .....	4
References .....	5
Policy History .....	8

## Hyperlink to Related Coverage Policies

- Cryoablation for Prostate Cancer
- Gene-Based Testing for Prostate Cancer Screening, Detection and Disease Monitoring
- Inpatient Admission for Radiation Therapy Intensity-Modulated Radiation Therapy (IMRT)
- Intraoperative Radiation Therapy
- Neutron Beam Therapy
- Prostate Saturation Biopsy
- Prostate-Specific Antigen (PSA) Screening for Prostate Cancer
- Proton Beam Therapy for Prostate Cancer
- Stereotactic Radiosurgery
- Transrectal Ultrasound (TRUS)
- Tumor Markers for Diagnosis and Management of Cancer

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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 brachytherapy as medically necessary for the treatment of localized prostate cancer.**

## General Background

Approximately one in every six men older than 50 years of age will be diagnosed with prostate cancer. It is currently the most frequently diagnosed malignancy among men, and the second leading cancer cause of death. A wide variety of treatments are available for prostate cancer. These treatments include radical

prostatectomy, active surveillance (i.e., watchful waiting), hormone therapy/androgen deprivation therapy (ADT), low- and high-dose-rate brachytherapy, chemotherapy, and radiation therapy.

Brachytherapy, also known as interstitial brachytherapy, involves placing radioactive sources into the prostate tissue. Brachytherapy uses either permanent implantation or temporary implantation. In permanent implantation, the radioactive sources remain in the tissues, whereas in temporary implantation, the radioactive sources are removed after the desired radiation dose is achieved. Brachytherapy is also described by the rate at which the dose is delivered, known as the dose rate. The International Commission on Radiation Units & Measurements refers to a dose rate of 40 to 200 centigray (cGy) per hour (cGy/h) as a low-dose-rate (LDR), 200 to 1200 cGy/h as a moderate-dose-rate, and greater than 1200 cGy/h as a high-dose-rate (HDR). Permanent brachytherapy for prostate cancer, commonly referred to as prostate seed implantation, uses either iodine 125 (<sup>125</sup>I) or palladium 103 (<sup>103</sup>Pd) as radioactive sources for cases involving LDR. In contrast, HDR brachytherapy for prostate cancer uses the temporary placement of a high-activity iridium 192 (<sup>192</sup>Ir) radioactive source, which delivers a high radiation dose over a short period. Most centers use permanent implants, where the sources are implanted into the prostate and gradually lose their radioactivity. Because of the short range of the irradiation emitted from these low-energy sources, adequate doses levels can be delivered to the cancer within the prostate, while avoiding excessive irradiation of the bladder and rectum. Very high doses are not possible with brachytherapy because the radiation is delivered at a much slower dose rate than with external beam radiation therapy (EBRT), which reduces biological effectiveness. Current brachytherapy techniques attempt to improve the radioactive seed placement and radiation dose distribution.

Prostate brachytherapy as monotherapy is a treatment option for early, clinically organ-confined prostate cancer (cT1c–T2a, Gleason grade 2–6, prostate-specific antigen [PSA] <10 nanograms per milliliter [ng/mL]). (See Appendix for definitions of TNM Staging System and Gleason Grading System). Permanent brachytherapy as monotherapy is indicated for patients with low-risk cancers. For intermediate-risk cancers, brachytherapy may be combined with EBRT with or without neoadjuvant ADT, but the complication rate increases. Patients with high-risk cancers are generally considered poor candidates for permanent brachytherapy; however with the addition of EBRT and neoadjuvant ADT, brachytherapy may be effective in select patients. Patients with a very large or very small prostate, symptoms of bladder outlet obstruction, or a previous transurethral resection of the prostate (TURP) are not ideal candidates for brachytherapy (National Comprehensive Cancer Network [NCCN], 2009; Pisansky, et al., 2008).

### **U.S. Food and Drug Administration (FDA)**

The FDA approves a radionuclide brachytherapy source as a 510(k) Class II therapeutic, radiology device.

### **Literature Review**

Long-term study outcomes address cancer recurrence or metastasis, including biochemical relapse (PSA level increases after radiation therapy). Biochemical relapse typically occurs several years before there is clinical, biopsy, or radiologic evidence of cancer recurrence. Freedom from biochemical relapse is an indication that cancer is absent, or possibly present but not actively growing or spreading. Studies in the peer-reviewed literature therefore generally report outcomes of biochemical control rates and survival.

**Low-dose-rate (LDR) Brachytherapy:** LDR brachytherapy has become a mainstream treatment option with excellent long-term treatment outcomes in low-, intermediate-, and high-risk patients. Low-risk and intermediate-risk prostate cancer LDR brachytherapy may be given alone (monotherapy) or in combination with other therapies. In a systematic review, Koukourakis et al. (2009) reported the rate of durable biochemical control ranges from 87% to 94% for individuals with low-risk prostate cancer at ten years of follow up. For individuals with intermediate-risk prostate cancer—generally those with a Gleason score of 7, a PSA value 10, or a palpable stage T2b tumor—at approximately seven or more years, the reported biochemical control rate ranges from approximately 70% to 95%. Long-term studies report excellent overall survival and biochemical control with minimal toxicity (Koontz, et al., 2009; Sylvester, et al., 2007; Stock, et al., 2006; Potters, et al., 2005; Critz and Levinson, 2004). For individuals with high-risk prostate cancer, LDR brachytherapy is generally given in conjunction with other therapies. Koukourakis et al. (2009) reported the practice of combining brachytherapy with EBRT has resulted in excellent biochemical control rates and 5-7 year survival rates with minimal toxicity. Although not always statistically significant, studies report superior results with combination brachytherapy and EBRT than with EBRT alone (Koontz, et al., 2009; Prada, et al., 2008; Merrick, et al., 2007; Sylvester, et al., 2007; Sathya, et al., 2005; Stock et al 2006; Sharkey, et al., 2005).

**High-dose-rate (HDR) Brachytherapy:** As is the case with LDR brachytherapy, HDR brachytherapy may be given alone (monotherapy) or in combination with other therapies, and studies in the peer-reviewed literature generally report outcomes of biochemical control rates and survival. Again similar to LDR brachytherapy, the greatest clinical experience with HDR brachytherapy for prostate cancer involves its combination with EBRT. Demanes et al. (2009) prospectively evaluated 411 patients who received HDR brachytherapy and EBRT and were followed for a median of 6.4 years. The overall 10-year biochemical control rate was 81%; stratified by risk group control rates, these results were low-risk 92%, intermediate-risk 87%, and high-risk 63%. Hoskin et al. (2007) conducted a randomized controlled trial including 218 patients with localized prostate cancer. A total of 109 received HDR brachytherapy with EBRT and 109 received EBRT only. Patients were followed for median of 30 months. The authors reported that a statistically significant advantage for the HDR treatment was seen; mean PSA relapse-free survival in the HDR arm was 5.1 years compared to 4.3 years in the control arm. Phan et al. (2007) retrospectively reported on 309 patients treated with HDR brachytherapy and EBRT who were followed for a median of 59 months. The 5-year biochemical control rate was 86%, and overall survival was 91%. Biochemical control in stratified into low-, intermediate- and high-risk groups was 98%, 90% and 78%, respectively. Yamaga et al. (2006) retrospectively reported on 105 patients treated with HDR brachytherapy and EBRT who were followed for a median of 44 months. The 5-year PSA relapse-free survival outcomes for low-, intermediate- and high-risk patients were 100%, 98%, and 92%, respectively. Yoshioka et al. (2006) conducted a prospective trial, treating 111 localized prostate cancer patients (15 low-risk, 28 intermediate-risk, and 68 high-risk) with HDR brachytherapy monotherapy. The 3-year local control, overall survival, and PSA failure-free rates were 100%, 97%, and 83%, respectively. The corresponding 5-year rates were 97%, 92%, and 70%. No Grade 4 or 5 late toxicity was detected; Grade 3 late toxicity was detected in one patient (1%). The authors noted their study demonstrated acceptable toxicity and promising short-term tumor control, even for locally advanced cases. Grills et al. (2004) prospectively evaluated 149 early stage prostate cancer patients treated with brachytherapy (65 patients with HDR, 84 patients with LDR). Median follow up for all patients was 35 months. Biochemical control was 97% and 98% for LDR and HDR, respectively. HDR brachytherapy was associated with statistically significant decreases in the rates of dysuria, as well as urinary frequency and/or urgency.

## **Professional Societies/Organizations**

### **American Brachytherapy Society (ABS)**

**Low-dose-rate Brachytherapy:** ABS inclusion criteria for low-dose brachytherapy in prostate cancer are:

- Life expectancy greater than five years
- Clinical stage: T1b–T2c and selected T3
- Gleason score 2–10
- PSA: in almost all cases, a PSA  $\leq$  50 ng/ml
- No pathological evidence of pelvic lymph node involvement
- No distant metastases

Patient selection for monotherapy:

- Clinical stage T1b–T2b and Gleason score  $\leq$  6 and PSA  $\leq$  10ng/ml
- Select higher risk patients
- Salvage of select radiation therapy failures

Patient selection for boost therapy:

- Clinical stage T2c or greater and/or Gleason score  $\geq$  7 and/or PSA > 10ng/ml

Inadequate information exists to recommend supplemental external radiation therapy based on perineural invasion, percent positive biopsies and/or MRI-detected extracapsular penetration (ABS, not dated).

**High-dose-rate Brachytherapy:** The ABS inclusion criteria for high-dose brachytherapy in prostate cancer are:

- Clinical Stage: T1-T3b and selected T4
- Gleason Score: 2-10
- PSA: No upper limit, but in almost all cases, patient does not have documented distant metastasis (TxN0M0)

Relative Contraindications: severe urinary obstructive symptoms, extensive TURP defect or TURP within 6 month, collagen vascular disease.

Patient selection criteria for monotherapy:

- Clinical T1b-T2b and Gleason score  $\leq$  7 and PSA  $\leq$  10 ng/mL

Patient selection criteria for boost:

- Patients with high-risk features such as T3-T4, Gleason score 7-10, and/or PSA > 10 ng/mL
- Selected patients with “bulky” T1-2b tumor (inadequate information exists to clearly define bulky tumor based on DRE, TRUS, percentage positive biopsies) (ABS, 2008).

### **American Urological Association (AUA)**

The AUA guideline for the treatment of patients with clinically localized prostate cancer (2007, reconfirmed 2009) indicates that a patient with clinically localized prostate cancer should be informed about the commonly accepted initial treatments including, at a minimum, active surveillance, radiotherapy (external beam and interstitial), and radical prostatectomy. A discussion of the estimates for benefits and harms of each intervention should be offered to the patient.

- Treatment for the Low-risk patient (PSA ≤ 10ng/ml and Gleason score ≤ 6, and clinical stage T1c or T2a): Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy, and radical prostatectomy are appropriate monotherapy treatment options.
- Treatment for the Intermediate-risk patient (PSA > 10–20 ng/ml or Gleason score of 7 or clinical stage T2b but not qualifying for high-risk): Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy, and radical prostatectomy are appropriate treatment options.
- Treatment for the High-risk patient (PSA >20ng/ml or Gleason score 8–10 or clinical stage T2c): Although active surveillance, interstitial prostate brachytherapy, external beam radiotherapy, and radical prostatectomy are options for the management of patients with high-risk localized prostate cancer; recurrence rates are high.

### **National Comprehensive Cancer Network (NCCN)**

The NCCN Prostate Cancer Guidelines (v.3.2010) suggest use of the brachytherapy for the treatment of prostate cancer as follows:

- Permanent brachytherapy as monotherapy is indicated for patients with low-risk cancers.
- For intermediate-risk cancers, consider combining brachytherapy with EBRT ± neoadjuvant/ concomitant/adjuvant androgen deprivation therapy.
- Patients with high-risk cancers are generally considered poor candidates for permanent brachytherapy; however, with the addition of EBRT and androgen deprivation therapy, it may be effective in some patients.
- Patients with a very large prostate or very small prostate, symptoms of bladder outlet obstruction or a previous transurethral resection of the prostate (TURP), are more difficult to implant and may suffer increased risk of side effects. Neoadjuvant androgen deprivation therapy may be used to shrink the prostate to an acceptable size.

### **Summary**

Evidence in the published peer-reviewed scientific literature supports the use of brachytherapy, both low-dose-rate (LDR) and high-dose-rate (HDR), as a safe and effective treatment for localized prostate cancer. Brachytherapy alone or combined with other modalities, has become a standard of care within the armamentarium of prostate cancer treatments.

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## **Coding/Billing Information**

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

**Covered when medically necessary:**

<b>CPT<sup>®</sup>* Codes</b>	<b>Description</b>
55875	Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy
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)
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

ICD-9-CM Diagnosis Codes	Description
185	Malignant neoplasm of prostate
233.4	Carcinoma in situ of prostate

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

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## APPENDIX

### The TNM Staging System

The TNM Staging System is based on the extent of the tumor (T), the extent of spread to the lymph nodes (N), and the presence of metastasis (M).

The T category describes the original (primary) tumor.

TX	Primary tumor cannot be evaluated
T0	No evidence of primary tumor
Tis	Carcinoma in situ (early cancer that has not spread to neighboring tissue)
T1–T4	Size and/or extent of the primary tumor

The N category describes whether or not the cancer has reached nearby lymph nodes.

NX	Regional lymph nodes cannot be evaluated
NO	No regional lymph node involvement (no cancer found in the lymph nodes)
N1-N3	Involvement of regional lymph nodes (number and/or extent of spread)

The M category tells whether there are distant metastases (spread of cancer to other parts of the body).

MX	Distant metastasis cannot be evaluated
MO	No distant metastasis (cancer has not spread to other parts of the body)
M1	Distant metastasis (cancer has spread to distant parts of the body)

Each cancer type has its own classification system, so letters and numbers do not always mean the same thing for every kind of cancer. Once the T, N, and M are determined, they are combined, and an overall "Stage" of I, II, III, IV is assigned. Sometimes these stages are subdivided as well, using letters such as IIIA and IIIB. (Source: American Joint Committee on Cancer, 2008)

### Gleason Grading System

The Gleason grading system accounts for the five distinct patterns that prostate tumor cells tend to go through as they change from normal cells. The scale runs from 1 to 5, where 1 represents cells that are very nearly normal, and 5 represents cells that don't look much like prostate cells at all. After examining the cells under a microscope, the pathologist looking at the biopsy sample assigns one Gleason grade to the most common pattern, and a second Gleason grade to the next most common pattern. The two grades are added, and the Gleason score, or sum, is determined. Generally speaking, the Gleason score tends to predict the

aggressiveness of the disease and how it will behave. The higher the Gleason score, the less the cells behave like normal cells, and the more aggressive the tumor tends to be. (Source: Prostate Cancer Foundation, 2009)

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## Policy History

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<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	11/15/2007	0419	Brachytherapy for Prostate Cancer

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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA’s subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.