



CIGNA MEDICAL COVERAGE POLICY

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

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Subject **Neutron Beam Therapy**

Table of Contents

| | |
|----------------------------------|---|
| Coverage Policy | 1 |
| General Background | 1 |
| Coding/Billing Information | 4 |
| References | 4 |
| Policy History | 7 |

Hyperlink to Related Coverage Policies

- Brachytherapy for Breast Cancer
- Brachytherapy for Gynecological Cancers
- Brachytherapy for Prostate Cancer
- Cryoablation for Prostate Cancer
- Photodynamic Therapy for Cancer
- Proton Beam Therapy for Lung Cancer
- Proton Beam Therapy for Prostate Cancer

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer'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 customer'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 customer'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 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 ©2011 CIGNA.

Coverage Policy

CIGNA covers neutron beam therapy as medically necessary for the treatment of inoperable, unresectable, or locally advanced malignant tumors of the salivary gland when there is failure, contraindication or intolerance to conventional methods of treatment.

CIGNA does not cover neutron beam therapy for any other indication because it is considered experimental, investigational or unproven.

General Background

Neutron beam therapy (NBT), also called fast neutron therapy, is a form of external beam radiation therapy that has a greater biologic impact on target cells than conventional photon radiation therapy. It has been proposed as an alternative to conventional therapy or for use in combination with photon therapy (i.e., mixed beam radiation therapy [MBT]), proton beam therapy and/or chemotherapy.

NBT delivers 20–100 times more energy than photon radiation, making it potentially more effective in photon-resistant tumors. Unlike photon therapy, neutron therapy prevents rebuilding of the deoxyribonucleic acid (DNA) of the tumor, halting the tumor growth. The physical properties of the neutron particles allow for precise dose localization and greater depth dose distribution than photon therapy. As a result, NBT typically requires fewer

treatments over a shorter length of time. However, it is reported that NBT causes more normal tissue damage than photon therapy.

NBT is administered at a treatment facility equipped with a superconducting accelerator (i.e., cyclotron). Treatment planning usually involves computed tomography (CT) to locate the tumor and determine its volume. Whether the patient receives NBT alone or in combination with conventional radiotherapy, the total dose is administered as a series of lower-dose daily fractions, 4–5 times per week for 5–7 weeks. In the case of mixed beam therapy, radiation treatment generally alternates between 2–3 days of NBT and 2–3 days of photon radiation per week. Treatment verification with a diagnostic x-ray may be required at each visit. Patients require radiological and clinical surveillance to confirm treatment success and to monitor for possible complications and/or tumor recurrence.

NBT is a recognized treatment option for inoperable, unresectable, or locally advanced malignant tumors of the salivary gland. However, evidence in the published peer reviewed scientific literature does not support NBT for the treatment of other cancers including, but not limited to locally advanced head and neck tumors, prostate cancer, soft tissue sarcomas, small-cell lung cancer, and breast cancer.

U.S. Food and Drug Administration (FDA)

The equipment used to deliver neutron beam therapy is approved as a Class II, 510(k) device by the FDA. An example is the Neutron Therapy System (Northern Illinois University Institute, DeKalb, IL). This device is “designed to produce and deliver a neutron beam for the treatment of patients with localized tumors and other conditions susceptible to treatment by radiation” (FDA, 2007).

Salivary Gland Cancer

Salivary gland cancer may involve the major (i.e., parotid glands, submandibular glands, and sublingual glands) or the minor salivary glands. The standard treatment for salivary gland cancer is surgical removal. Chemotherapy may be an effective treatment modality for low-grade tumors. Conventional radiation therapy can be used as an adjuvant to surgery when positive margins are present and in some cases, may be the first line of treatment. NBT is an established treatment option for inoperable, unresectable, or locally advanced salivary gland tumors (ACS, 2010; National Cancer Institute [NCI], Nov 2010).

Literature Review: There is a paucity of evidence in the form of case series and retrospective reviews including small, heterogeneous patient populations (n=16–279) with diverse tumors occurring in a variety of primary sites. The studies included patients with gross residual disease and/or inoperable, recurrent, incompletely resected tumors. Most patients had been unsuccessfully treated with conventional therapy prior to treatment with NBT. The outcomes of these studies reported a 67%, six-year survival rate (Douglas, et al., 2003) to an 85%, 15-year actuarial survival rate (Douglas, et al., 2001). Huber et al. (2001) reported that although there was no significant difference in the survival rates of patients treated with NBT compared to mixed beam therapy, there was a significant advantage in local control.

The Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS, 2003) published a technology brief on neutron therapy for the treatment of salivary gland tumors. AETMIS stated that NBT is a well established treatment for inoperable and unresectable tumors, and is the treatment of choice, especially for unresectable cystic adenoid carcinomas of the main or accessory salivary glands. For advanced stage tumors, treatment is palliative. NBT is also a treatment option following surgical intervention for large-volume residual diseases. AETMIS further stated that there is a “paucity of efficacy data on neutron therapy.”

Professional Societies/Organizations: The National Comprehensive Cancer Network[®] Clinical Practice Guidelines in Oncology[™] (2011) list photon/electron therapy or neutron therapy as definitive radiation therapy options for salivary gland tumors. NCCN also lists neutron therapy as a postoperative treatment option.

The National Cancer Institute (Nov 2010) stated that fast neutron beams have been reported to improve disease-free and overall survival rates in patients with stage I, low-grade major salivary tumors with poor prognosis and grade II-III tumors that are inoperable, unresectable, or recurrent.

Other Head and Neck Carcinomas

Other head and neck cancers include cancers of the oral cavity, paranasal sinuses, nasal cavity, pharynx, larynx, and lymph nodes in the upper part of the neck. The treatment of these cancers depends on the location,

stage of cancer, and the patient's age and morbidities. Treatment modalities include surgical excision, radiation therapy, and/or chemotherapy, Neutron beam therapy is not an established treatment option for other head and neck cancers (NCCN, 2011; NCI, 2005).

Literature Review: Glenny et al. (2010) conducted a systematic review of randomized controlled trials (RCTs) to “determine which radiotherapy regimens for oral cavity and oropharyngeal cancers resulted in increased overall survival, disease free survival, progression free survival and locoregional control.” Five NBT studies met inclusion criteria. One RCT (n=327) compared mixed beam therapy to conventional therapy and reported no statistically significant differences in total mortality or locoregional control. Four additional RCTs compared NBT to photon therapy (n=531). No statistically significant differences were reported in total mortality, locoregional control and/or disease free survival in these studies. The authors noted that the trials were at unclear or high risk of bias for subjective outcomes.

In a prospective case series, Stelzer et al. (2008) treated ten patients with glioblastoma multiforme or gliosarcoma with neutron therapy using three-dimensional treatment planning. Median survival was 55 weeks, median progression-free survival was 16 weeks, one-year survival was 60%, and one patient remained alive at 255 weeks. All ten patient failed by 39 weeks demonstrating tumor progression on MRI. No grade three or higher toxicities were reported. The authors noted that previous NBT studies were plagued by neurotoxicity with no improvement in survival, and that the overall and progression-free survival rate trends were better using photon therapy. Earlier studies in the form of randomized controlled trials (Maor, et al., 1995; MacDougall, et al., 1990; Duncan, et al., 1987) compared mixed beam therapy to conventional therapy and reported no significant differences in tumor control or five-year survival rates and in some cases, higher complication rates occurred with NBT.

Prostate Cancer

Cancer of the prostate is a tumor that occurs predominantly in older men, may be cured when localized, and frequently responds well to treatment when widespread. Treatment options include active surveillance (i.e., watchful waiting), surgical intervention, cryoablation, radiation therapy, hormonal therapy or androgen deprivation therapy and cryotherapy (National Cancer Institute [NCI], Dec 2010).

Literature Review: Many of the studies investigating the treatment of prostate cancer with NBT were conducted prior to the year 2000 and included randomized controlled trials (Laramore, et al., 1993; Krieger, et al., 1989; Russell, et al., 1987), case series (Hart, et al., 1996; Cohen, et al., 1995; Russell, et al., 1994); and retrospective reviews (Forman, et al., 1999; Soulen, et al., 1997; Chuba, et al., 1996; Haraf, et al., 1995; Austin-Seymore, et al., 1994). The studies evaluated NBT only or mixed beam therapy with various dosages, small patient populations, and short term follow-ups. Outcomes from randomized controlled trials were similar in patients treated with NBT compared to photon conventional therapy, but the results of the studies indicated that the therapeutic gain from NBT was offset by similar distant metastasis rates and late complications rates as high as 51%.

Soft Tissue Sarcomas

Soft tissue sarcomas are malignant tumors that arise from the mesodermal tissues of the extremities, trunk, retroperitoneal, and head and neck areas. Treatment depends on the tumor characteristics. Surgical incision may completely obliterate a low-grade tumor. Higher grade tumors require more extensive, reconstructive surgery, often in combination with radiation therapy with or without chemotherapy (NCI, Apr 2011; Huber, et al., 2006).

Literature Review: Studies investigating NBT for soft-tissue sarcoma are primarily in the form of case series (Fontanesi, et al., 2005) and retrospective reviews (Schwartz, et al. 2001; Schönekaes, et al., 1999) with small heterogeneous patient populations, short-term follow-ups, and the use of various radiation dosages. There is insufficient data to support PBT for the treatment of these tumors.

Professional Societies/Organizations: The National Cancer Institute (NCI, Apr 2011) lists fast neutron therapy as one of several standard treatment options for Stage I adult soft tissue sarcomas.

Other Cancers

The published peer reviewed scientific literature includes studies that have also investigated NBT for the treatment of gliomas, gynecological cancers, esophageal cancers, breast cancer, bladder cancer, non-small cell

lung cancer, and adenoid cystic carcinoma of the trachea. There is ongoing controversy regarding the safety and effectiveness of NBT for other cancers. Advocates propose that NBT is a more efficient treatment than other alternatives, but based on small patient populations, high complication rates, contrasting outcomes when compared with historical data, high cost and limited availability of neutron facilities, its therapeutic value has not been established (Maucort-Boulch, et al., 2010; Bittner, et al., 2008; Smith, et al., 2006; Bell, et al., 2005).

Maucort-Boulch et al. (2010) conducted a meta-analysis of NBT for the treatment of high-grade gliomas (i.e., grades III-IV). Four randomized controlled trials (n=316) met inclusion criteria and compared NBT alone or NBT with photon therapy to photon therapy alone. Overall mortality data was available at 12 and 24 months. A 7% increase (range 5% decrease to 20% increase) in mortality was seen at the 12-months and a 6% increase (range 3% decrease to 15% increase) in mortality was seen at 24 months following NBT. NBT did not improve the survival of patients with high-grade gliomas.

Summary

Although the overall body of evidence in the published peer-reviewed scientific literature is not robust, neutron beam therapy (NBT) is an established treatment option for inoperable, unresectable, or locally advanced malignant tumors of the salivary gland when conventional therapies fail, are contraindicated or not tolerated. The safety and efficacy of NBT for the treatment of other forms of cancer have not been proven.

Coding/Billing Information

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

Covered when medically necessary and used to report neutron beam therapy for malignant neoplasms of the salivary glands:

| CPT ^{®*} Codes | Description |
|-------------------------|---|
| 77422 | High energy neutron radiation treatment delivery; single treatment area using a single port or parallel-opposed ports with no blocks or simple blocking |
| 77423 | High energy neutron radiation treatment delivery; 1 or more isocenter(s) with coplanar or non-coplanar geometry with blocking and/or wedge, and/or compensator(s) |

| ICD-9-CM Diagnosis Codes | Description |
|--------------------------|--|
| 142.0-142.9 | Malignant neoplasms of the salivary glands |
| 145.9 | Malignant neoplasm of mouth, unspecified site |
| 330.0 | Carcinoma in situ of lip, oral cavity, and pharynx |

Experimental/Investigational/Unproven/Not Covered:

| ICD-9-CM Diagnosis Codes | Description |
|--------------------------|-----------------|
| | All other codes |

*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 | 06/15/2008 | 0251 | Neutron Beam Therapy |

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