# MEDICAL POLICY

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| MEDICAL POLICY DETAILS | |
|---|---|
| **Medical Policy Title** | **Proton Beam Radiation Therapy** |
| **Policy Number** | **6.01.11** |
| **Category** | **Technology Assessment** |
| **Original Effective Date** | **07/02/99** |
| **Committee Approval Date** | **04/19/01, 07/18/02, 07/17/03, 06/17/04, 05/18/05, 03/16/06, 01/18/07, 12/20/07, 01/15/09, 03/18/10, 03/17/11, 02/16/12, 02/21/13, 02/20/14, 06/19/14, 02/19/15, 04/21/16, 06/15/17, 04/19/18, 05/16/19, 04/16/20, 04/15/21, 04/21/22, 06/16/22** |
| **Current Effective Date** | **06/16/22** |
| **Archived Date** | **N/A** |
| **Archive Review Date** | **N/A** |
| **Product Disclaimer** | • *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.*<br>• *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.*<br>• *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.*<br>• *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.*<br>• *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service please refer to the Medicaid Product coverage line.* |

## POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, charged particle irradiation with proton ion beams has been medically proven to be effective and therefore, is considered a **medically appropriate** treatment for the following indications:
   A. Primary therapy for melanoma of the uveal tract (iris, choroid, or ciliary body), with no evidence of metastasis or extrascleral extension, and with tumors up to 24 mm in largest diameter and 14 mm in height; or
   B. Post-operative therapy (with or without conventional high-energy x-rays) in patients who have undergone biopsy or partial resection of the chordoma or low-grade (I or II) chondrosarcoma of the basisphenoid region (skull-base chordoma or chondrosarcoma) or cervical spine. Patients eligible for this treatment have residual localized tumor without evidence of metastasis; or
   C. Localized unresectable hepatocellular carcinoma, when considered preferential to stereotactic body radiation Therapy (SBRT) or radiofrequency ablation; or
   D. Treatment of pediatric central nervous system tumors; or
   E. Thymoma and Thymic Cancer

II. Based upon our criteria and assessment of the peer reviewed literature, charged particle irradiation with proton ion beams has not been medically proven to be effective and, therefore, is considered **not medically necessary** for all other indications, including but not limited to prostate cancer, non-small-cell lung cancer, and esophageal cancer.

*Refer to Corporate Medical Policy #6.01.12 Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy.*

*Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services.*

*Refer to Corporate Medical Policy #11.01.10 Clinical Trials.*

*Refer to Corporate Medical Policy #11.01.13 Out of Area/Out of Network Services.*

## POLICY GUIDELINE

Proton beam radiation therapy (PBT) is only covered when performed in specialized centers. There are numerous centers operating in the United States and additional being planned or under construction (Please refer to the website of the National Association of Proton Centers (https://www.proton-therapy.org/map/).

## DESCRIPTION

Charged particle beams consisting of protons or helium ions are an alternative to conventional x-rays, and other types of photon irradiation in the treatment of malignant disease. When positively charged atomic particles called protons travel through tissue, they have a limited range, depending on the power of the proton beam. As they reach the end of their range, protons release a burst of energy within a very limited area. Controlling the power of the beam allows delivery of radiation to the tumor, but not to tissues lying behind the tumor, thereby minimizing radiation exposure to surrounding normal tissue. PBT requires specialized equipment in the form of accelerators (cyclotrons, synchrotrons, synchrocyclotrons, or linear accelerators) that can generate a beam of particles (protons or helium ions). PBT also requires accurate localization of the malignancy by using tomographic scanning (with x-ray and/or magnetic resonance imaging), precise and reproducible positioning (relative to the beam) and immobilization of the patient during both tomographic scanning and treatment.

PBT is a form of radiation therapy that can be used for either stereotactic radiosurgery or conventional fractionated radiation therapy. It can also be used without stereotactic guidance.

Radiation therapy with charged-particle beams such as protons may be recommended when:

I. Conventional treatment modalities do not provide adequate local tumor control;

II. The likelihood of metastasis prior to radiotherapy is small to nonexistent;

III. There is evidence that local tumor response depends on the dose of radiation delivered; or

IV. Delivery of an adequate radiation dose to the tumor is limited by the proximity of vital radiosensitive tissues or structures.

## RATIONALE

Radiotherapy is a procedure and therefore is not subject to U.S. Food and Drug Administration (FDA) regulations. However, the accelerators and other equipment used to generate and deliver charged particle radiation are devices, and thus do require FDA approval. The equipment used to deliver PBT is approved as a Class II, 510(k) device by the FDA.

Uveal melanoma, chordoma, or chondrosarcoma of the skull base or cervical spine. Clinical evidence supports that PBT improves health outcomes for patients with uveal melanoma and with chordoma or chondrosarcoma of the skull base or cervical spine. Most of these patients have few other treatment options. A small case series of patients with recurrent uveal melanoma indicated that a second course of PBT was associated with a relatively good probability of local control and a low enucleation rate.

Hepatocellular cancer. In hepatocellular cancer, radiation therapy plays a role in patients with unresectable cancers and in those patients not amenable to radiofrequency ablation. Stereotactic body radiation therapy (SBRT) has been used as well as PBT. The larger PBT series, which are from Japan, suggest excellent local control rates and modest two-to-five-year survival rates. Four retrospective studies (360 patients) and two prospective studies (64 patients) of PBT in patients with hepatocellular cancer show results similar to those achieved with SBRT. In patients with unresectable hepatocellular cancers who are not optimally treated with radiofrequency ablation or SBRT, PBT is considered medically necessary.

Pediatric central nervous system cancers. A 2016 systematic review by Leroy et al., identified several case series evaluating PBT for several types of pediatric central nervous system (CNS) tumors including craniopharyngioma,

ependymoma, medulloblastoma, and CNS germinoma. Twenty-three primary studies were identified, with approximately 650 patients overall. The median/mean follow-up times were limited (range, 19-91 months). None of the studies were randomized; two were comparative, and 20 were retrospective. Most of the studies suffered from serious methodologic limitations, yielding a very low level of clinical evidence for the outcomes in all indications. Although there is no doubt that PBT reduces the radiation dose to normal tissues and organs, there was insufficient evidence to either support or refute the use of PBT in children.

Prostate cancer. Data published concerning the use of PBT in large numbers of patients with localized prostate cancer results comparable to those obtained with alternative techniques. A 2008 comparative effectiveness review of therapies for clinically localized prostate cancer by the Agency for Healthcare Research and Quality (AHRQ) indicated that, based on nonrandomized comparisons, the absolute rates of outcomes after proton radiation appear similar to other treatments. However, the clinical utility of dose escalation using PBT, compared to doses similar to those currently used in intensity modulated radiation therapy (IMRT) (e.g.,79-81 Gy), is still not known and further studies are needed. The American Society for Radiation Oncology (ASTRO) published a guideline for clinically localized prostate cancer in 2017 which states, “limited information exists in relation to the comparative effectiveness of proton therapy compared to other radiation techniques or other modalities of treatment. Clinicians should inform localized prostate cancer patients who are considering proton beam therapy that it offers no clinical advantage over other forms of definitive treatment” (Moderate Recommendation; Evidence Level: Grade C).

Thymomas and thymic carcinomas.Thymomas and thymic carcinoma, also collectively referred to as thymic epithelial tumors (TETs), are very rare neoplasms (0.13 cases per 100,000 person years) located in the anterior mediastinum. Thymomas specifically are associated with autoimmune paraneoplastic diseases (e.g., myasthenia gravis, hypogammaglobulinemia, autoimmune pure red cell aplasia) but the clinical behavioral of all TETs can vary greatly from indolent to metastatic and aggressive, with a five-year survival for inoperable locally advanced carcinoma of 36%; and 24% for metastatic thymoma and thymic carcinoma. The anterior mediastinum holds the heart, lungs, and esophagus, critical organs that are areas of concern for toxicity following radiation therapy, including the risk for secondary malignancies, cardiovascular disease, hypothyroidism, cerebrovascular accidents, pulmonary sequelae, and muscle atrophy.

Given the rare nature of the disease, literature is limited to small case and cohort studies. A 2016 dosimetry comparison by Parikh, et al, demonstrated that PBT delivered significantly lower mean doses of radiation to the lung (.61 Gy vs. 8.13 Gy; P=0.2), esophagus (5.39 vs 20.62 Gy; P=.003) and heart (6.00 vs 10.44 Gy; P=.007) when compared to intensity modulated radiation therapy (IMRT), while adjuvantly treating thymomas in 4 patients at a single proton therapy center.

The NCCN V2.2022 guidelines for thymomas and thymic carcinomas were updated to consider proton therapy use as appropriate, and state that compared to IMRT, it has been shown to improve the dosimetry allowing better sparing of the normal organs (lungs, heart, and esophagus) with favorable local control and toxicity, removing the verbiage, “for certain patients”. This is a Category 2A recommendation.

Other indications. Case series with small sample size that addresses PBT in the treatment of esophageal, non-small-cell lung cancer (NSCLC) and invasive bladder carcinoma indicate favorable results, but these studies have limitations of small sample size and short follow-up period. Small retrospective studies indicate that the use of PBT appears promising for the treatment of Stage I non-small-cell lung cancer; however, prospective clinical trials with larger study populations and longer follow-up periods are needed.

ASTRO has published a model policy, most recently updated in 2017. It states that PBT is considered reasonable in instances where sparing the surrounding normal tissue cannot be adequately achieved with photon-based radiotherapy and is of added clinical benefit to the patient. The policy lists four examples of when PBT might be preferred over conventional radiotherapy, which include reducing the potential for toxicity to critical nearby structures. In addition to meeting criteria in one of the four listed examples, the radiation oncologist must determine the patient’s suitability for PBT allowing for reproducible delivery, adequate definition of the target volumes and organs at risk; equipment capability; physician, physicist, and staff training; and adequate quality assurance procedures. Normal tissue dose volume histograms (DVHs) must be demonstrably improved with a PBT plan, to validate coverage. Coverage decisions must extend beyond ICD-10 codes to incorporate considerations of clinical scenario and medical necessity with appropriate

documentation, which may include comparative dose volume histograms. On the basis of the medical necessity requirements and published clinical data, disease sites that frequently support the use of PBT include the following: ocular tumors, including intraocular melanomas; tumors that approach or are located at the base of the skull (e.g., chordoma, chondrosarcomas); primary or metastatic tumors of the spine (where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has been previously irradiated); primary hepatocellular cancer and primary or benign solid tumors in children treated with curative intent and occasional palliative treatment, when at least one of four example criteria is met, malignant and benign primary CNS tumors, advanced (e.g.,T4) and/or unresectable head and neck cancers, cancers of the paranasal sinuses and other accessory sinuses, non-metastatic retroperitoneal sarcomas, and re-irradiation cases. PBT may also be appropriate for patients with genetic syndromes that make total volume of irradiation minimization crucial, such as, but not limited to NF-1 patients and retinoblastoma patients. PBT would be considered as part of "coverage with evidence development" (CED) for indications that include, but not limited to the following: non- T4 and resectable head and neck malignancies; thoracic malignancies; abdominal malignancies; and pelvic malignancies, including non-metastatic rectal, anal, bladder and cervical cancers, non-metastatic prostate cancer, and breast cancer. In the treatment of prostate cancer, the use of PBT is evolving as the comparative efficacy evidence is still being developed. PBT for primary treatment of prostate cancer should only be performed within the context of a prospective clinical trial or registry.

## CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

**CPT Codes**

| Code | Description |
|---|---|
| 77520 | Proton treatment delivery; simple, without compensation |
| 77522 | Proton treatment delivery; simple, with compensation |
| 77523 | Proton treatment delivery; intermediate |
| 77525 | Proton treatment delivery; complex |



**HCPCS Codes**

| Code | Description |
|---|---|
| No codes | |

**ICD10 Codes**

| Code | Description |
|---|---|
| C22.0-C22.8 | Malignant neoplasm of liver and intrahepatic bile ducts (code range) |
| C30.0-C31.9 | Malignant neoplasm of nasal cavity, middle ear, accessory sinuses (code range) |
| C40.80-C40.82 | Malignant neoplasm of overlapping sites of bone and articular cartilage of limb (code range) |
| C40.90-C40.92 | Malignant neoplasm of unspecified bones and articular cartilage of limb (code range) |
| C41.0-C41.9 | Malignant neoplasm of bone and articular cartilage of other and unspecified sites (code range) |

| Code | Description |
|---|---|
| C61 | Malignant neoplasm of prostate |
| C69.30-C69.42 | Malignant neoplasm of choroid or ciliary body (code range) |
| C72.20-C72.9 | Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system (code range) |
| C78.30-C78.39 | Secondary malignant neoplasm of other and unspecified respiratory organs (code range) |
| C79.32 | Secondary malignant neoplasm of cerebral meninges |
| C79.40-C79.49 | Secondary malignant neoplasm of other and unspecified parts of nervous system (code range) |
| C79.51-C79.52 | Secondary malignant neoplasm of bone or bone marrow (code range) |
| D02.3 | Carcinoma in situ of other parts of respiratory system |
| D07.5 | Carcinoma in situ of prostate |

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*Key Article

## KEY WORDS

Charged particle radiation therapy, conformal proton beam radiation, proton beam radiation, proton beam therapy, intensity-modulated proton beam therapy, pencil beam scanning.

## CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination (LCD) for Proton Beam Therapy. Please refer to the following LCD website for Medicare members: https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35075&ContrId=298&ver=34&ContrVer=1&CntrctrSelected=298*1&Cntrctr=298&s=41&DocType=1&bc=AAQAAAIAAAAA&