Medical Policy
Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions

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Policy Number: 437
BCBSA Reference Number: 8.01.10
NCD/LCD: Local Coverage Determination (LCD): Proton Beam Therapy (L35075)

Related Policies
Clinical Exception and Notification Form for Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions, #678
Intensity-Modulated Radiation Therapy (IMRT) of the Breast and Lung #163
Intensity-Modulated Radiation Therapy (IMRT) of the Prostate #090
Intensity-Modulated Radiation Therapy (IMRT): Abdomen and Pelvis #165
Intensity-Modulated Radiation Therapy (IMRT): Cancer of the Head and Neck or Thyroid #164
Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy #277

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Charged-particle irradiation with proton or helium ion beams may be considered MEDICALLY NECESSARY in the following clinical situations*:

- 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;
- Postoperative therapy (with or without conventional high-energy x-rays) in patients who have undergone biopsy or partial resection of 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.
- In the treatment of pediatric central nervous system tumors.

*Please note: Clinical Exception and Notification form must be filled out and submitted prior to all proton beam therapy treatments.
Other applications of charged-particle irradiation with proton or helium ion beams are considered **INVESTIGATIONAL**. This includes, but is not limited to:

- Clinically localized prostate cancer
- Non-small-cell lung cancer (NSCLC) at any stage or for recurrence,
- Pediatric non-central nervous system tumors,
- Tumors of the head and neck (other than skull-based chordoma or chondrosarcoma).

**Clinical Exception and Notification Form**
Providers must submit a request for an exception for a non-covered indication by completing the clinical exception and notification form. [Click here for the Proton Beam exception and notification form (#678)]

Providers must complete the Clinical Exception and Notification Form when requesting coverage:
- For medically necessary indications described in medical policy 437, Charged-Particle (Proton or Helium Ion) Radiation Therapy.
- For non medically necessary and investigational indications, described in medical policy 437, Charged-Particle (Proton or Helium Ion) Radiation Therapy.

The clinical exception/notification form is not required for Medicare Advantage members.

**Medicare HMO BlueSM and Medicare PPO BlueSM Members**

**Indications for Coverage**

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.

Examples of such an advantage might be:
1. The target volume is in close proximity to one or more critical structures and a steep dose gradient outside the target must be achieved to avoid exceeding the tolerance dose to the critical structure(s).
2. A decrease in the amount of dose inhomogeneity in a large treatment volume is required to avoid an excessive dose "hotspot" within the treated volume to lessen the risk of excessive early or late normal tissue toxicity.
3. A photon-based technique would increase the probability of clinically meaningful normal tissue toxicity by exceeding an integral dose-based metric associated with toxicity.
4. The same or an immediately adjacent area has been previously irradiated, and the dose distribution within the patient must be sculpted to avoid exceeding the cumulative tolerance dose of nearby normal tissue.

PBT may offer dosimetric advantages as well as added complexity over conventional radiotherapy, 3D Conformal Radiation Therapy (3-D CRT) or Intensity Modulated Radiation Therapy (IMRT). Before applying PBT techniques, a comprehensive understanding of the benefits and consequences is required. In addition to satisfying at least one of the four selection criteria noted above, the radiation oncologist's decision to employ PBT requires an informed assessment of the benefits and risks including:
- Determination of patient suitability for PBT allowing for reproducible treatment delivery
- Adequate definition of the target volumes and OARs
- Equipment capability, including ability to account for organ motion when relevant
- Physician, physicist and staff training
- Adequate quality assurance procedures.

It is important to note that normal tissue dose volume histograms (DVHs) must be demonstrably improved with a PBT plan to validate coverage. Therefore, coverage decisions must extend beyond ICD-10 codes to incorporate additional considerations of clinical scenario and medical necessity with appropriate documentation. The final determination of the appropriateness and medical necessity for PBT resides
with the treating radiation oncologist who should document the justification for PBT for each patient.

**Group 1**

On the basis of the above 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 skull, including but not limited to:
  - 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 previously been irradiated
- Unresectable benign or malignant central nervous system tumors to include but not be limited to primary and variant forms of astrocytoma, glioblastoma, medulloblastoma, acoustic neuroma, craniopharyngioma, benign and atypical meningiomas, pineal gland tumors, and arteriovenous malformations
- Primary hepatocellular cancer treated in a hypofractionated regimen
- Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors when at least one of the four criteria noted above apply
- Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients
- Pituitary neoplasm
- Advanced staged (e.g., T4) and/or unresectable malignant lesions of the head and neck
- Malignant lesions of the paranasal sinus, and other accessory sinuses
- Unresectable retroperitoneal sarcoma.

PBT is one of the acceptable forms of external beam radiation therapy that may be used to administer Stereotactic Body Radiation Therapy (SBRT) or Stereotactic Radiosurgery (SRS). When PBT is used to administer SBRT or SRS, the delivery and management codes relevant for SBRT or SRS apply, and the same clinical indications apply as for those treatment strategies.

**Group 2**

Coverage of proton beam therapy in Group 2 is limited to providers who have demonstrated experience in data collection and analysis with a history of publication in the peer-reviewed medical literature.

- Unresectable lung cancers and upper abdominal/peri-diaphragmatic cancers
- Advanced stage, unresectable pelvic tumors including those with peri-aortic nodes or malignant lesions of the cervix
- Breast cancers
- Unresectable pancreatic and adrenal tumors
- Skin cancer with macroscopic perineural/cranial nerve invasion of skull base
- Unresectable malignant lesions of the liver, biliary tract, anal canal and rectum
- Prostate cancer, without distant metastases
- Hodgkin or Non-Hodgkin Lymphoma involving the mediastinum or in non-mediastinal sites where PBT has the potential to reduce the risk of pneumonitis or late effects of radiation therapy (secondary malignancy, cardiovascular disease, or other chronic health conditions)
- Re-irradiation where prior radiation therapy to the site is the governing factor necessitating PBT in lieu of other radiotherapy.

**Prostate Cancer**

Coverage and payments of proton beam therapy for prostate cancer will require:

a. Physician documentation of patient selection criteria (stage and other factors as represented in the NCCN guidelines);

b. Documentation and verification that the patient was informed of the range of therapy choices, including risks and benefits.
Medical necessity criteria and coding guidance for Medicare Advantage members living in Massachusetts can be found through the link below.

**Local Coverage Determination (LCD): Proton Beam Therapy (L35075)**

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

**Prior Authorization Information**
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required. Yes indicates that prior authorization is required. No indicates that prior authorization is not required. N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th></th>
<th>Outpatient</th>
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<tbody>
<tr>
<td><strong>Commercial Managed Care (HMO and POS)</strong></td>
<td>See above clinical exception and notification form</td>
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<tr>
<td><strong>Commercial PPO and Indemnity</strong></td>
<td>See above clinical exception and notification form</td>
</tr>
<tr>
<td><strong>Medicare HMO BlueSM</strong></td>
<td>No</td>
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<tr>
<td><strong>Medicare PPO BlueSM</strong></td>
<td>No</td>
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**CPT Codes / HCPCS Codes / ICD Codes**
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>77520</td>
<td>Proton treatment delivery; simple, without compensation</td>
</tr>
<tr>
<td>77522</td>
<td>Proton treatment delivery; simple with compensation</td>
</tr>
<tr>
<td>77523</td>
<td>Proton treatment delivery; intermediate</td>
</tr>
<tr>
<td>77525</td>
<td>Proton treatment delivery; complex</td>
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**Description**
Charged-particle beams consisting of protons or helium ions are a type of particulate radiotherapy (RT). They contrast with conventional electromagnetic (ie, photon) RT due to several unique properties, including minimal scatter as particulate beams pass through tissue, and deposition of ionizing energy at precise depths (ie, the Bragg peak). Thus, radiation exposure of surrounding normal tissues is minimized. The theoretical advantages of protons and other charged-particle beams may improve outcomes when the following conditions apply:

- Conventional treatment modalities do not provide adequate local tumor control;
- Evidence shows that local tumor response depends on the dose of radiation delivered; and
- Delivery of adequate radiation doses to the tumor is limited by the proximity of vital radiosensitive tissues or structures.
The use of proton or helium ion RT has been investigated in 2 general categories of tumors/abnormalities. However, advances in photon-based RT such as 3-dimensional conformal radiotherapy, intensity-modulated radiotherapy, and stereotactic body radiotherapy allow improved targeting of conventional therapy:

1. Tumors located near vital structures, such as intracranial lesions or lesions along the axial skeleton, such that complete surgical excision or adequate doses of conventional RT are impossible. These tumors/lesions include uveal melanomas, chordomas, and chondrosarcomas at the base of the skull and along the axial skeleton.
2. Tumors associated with a high rate of local recurrence despite maximal doses of conventional RT. One tumor in this group is locally advanced prostate cancer (ie, stages C or D1 [without distant metastases], also classified as T3 or T4).

Advances in photon-based RT such as 3-dimensional conformal radiotherapy, intensity-modulated radiotherapy, and stereotactic body radiotherapy allow improved targeting of conventional therapy.

Proton beam therapy can be given with or without stereotactic techniques. Stereotactic approaches are frequently used for uveal tract and skull-based tumors. For stereotactic techniques, 3 to 5 fixed beams of protons or helium ions are used.

**Summary**

Charged-particle beams consisting of protons or helium ions are a type of particulate radiotherapy (RT). Treatment with charged-particle radiotherapy is proposed for a large number of indications, often for tumors that would benefit from the delivery of a high dose of radiation with limited scatter.

For individuals who have uveal melanoma(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. Systematic reviews, including a 1996 TEC Assessment and a 2013 review of randomized and nonrandomized studies, concluded that the technology is at least as effective as alternative therapies for treating uveal melanomas and is better at preserving vision. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have skull-based tumor(s) (ie, cervical chordoma, chondrosarcoma) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes observational studies and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 1996 TEC Assessment concluded that the technology is at least as effective as alternative therapies for treating skull-based tumors. A 2016 systematic review of observational studies found 5-year survival rates after proton beam therapy (PBT) ranging from 67% to 94%. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have pediatric central nervous system tumor(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series, nonrandomized comparative studies, and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. There are few comparative studies and studies tended to have small sample sizes. The available observational studies do not provide sufficient evidence on the efficacy of charged-particle therapy compared with other treatments (eg, intensity-modulated radiotherapy). The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2013 strongly supported the use of charged-particle radiotherapy for treating pediatric central nervous system tumors. This modality of treatment of pediatric central nervous system
(CNS) tumors has the potential to reduce long-term adverse effects (eg, damage to nearby normal CNS tissue, development of radiation-induced secondary tumors).

For individuals who have pediatric non-central nervous system tumor(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes dosimetric planning studies in a small number of patients. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. There is a lack of randomized and observational studies evaluating the efficacy and safety of the technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have localized prostate cancer who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes 2 RCTs and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 2010 TEC Assessment addressed the use of PBT for prostate cancer and concluded that it had not yet been established whether PBT improves outcomes in any setting for clinically localized prostate cancer. The TEC Assessment included 2 RCTs, only 1 of which included a comparison group of patients who did not receive proton PBT. No data on the use of PBT for prostate cancer published since 2010 would alter the conclusions of the TEC Assessment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have non-small-cell lung cancer who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 2010 TEC Assessment included 8 case series and concluded that the evidence is insufficient to permit conclusions about PBT for any stage of non-small-cell lung cancer. No subsequent randomized or nonrandomized comparative studies have been published. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have head and neck tumors other than skull-based who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes. The systematic review noted that the studies on charged-particle therapy were heterogenous in terms of type of particle and delivery techniques, and that there are no head-to-head trials comparing charged-particle therapy to other treatments. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Policy History**

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<tr>
<th>Date</th>
<th>Action</th>
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<tr>
<td>9/2016</td>
<td>BCBSA National medical policy review. Title updated to indicate “for Neoplastic Conditions.” References added. 9/1/2016</td>
</tr>
<tr>
<td>8/2016</td>
<td>Updated to include Local Coverage Determination (LCD): Proton Beam Therapy (L35075). Effective 8/22/2016.</td>
</tr>
<tr>
<td>5/2016</td>
<td>BCBSA National medical policy review. The second policy statement was corrected to use the same “or helium ion” language as the first policy statement. 5/1/2016</td>
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<tr>
<td>9/2015</td>
<td>Local Coverage Determination (LCD): Proton Beam Therapy (L31617 added. 9/2015</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Charged particle (proton or helium ion) irradiation for uveal melanoma and for chordoma or chondrosarcoma of the skull base or cervical spine. TEC Assessments 1996;Volume 11, Tab 1.


