Protocol

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

(80110)

(Formerly Charged-Particle [Proton or Helium Ion] Radiotherapy)

Medical Benefit		**Effective Date**: 07/01/17	**Next Review Date**: 03/18
Preauthorization	Yes	**Review Dates**: 03/09, 03/10, 03/11, 03/12, 03/13, 03/14, 03/15, 03/16, 03/17	

Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With uveal melanoma(s)	Interventions of interest are: • Charged-particle (proton or helium ion) radiotherapy	Comparators of interest are: • Plaque radiotherapy • Surgical resection • Transpupillary thermotherapy	Relevant outcomes include: • Overall survival • Disease-free survival • Change in disease status • Treatment-related morbidity
Individuals: • With skull-based tumor(s) (i.e., cervical chordoma, chondrosarcoma)	Interventions of interest are: • Charged-particle (proton or helium ion) radiotherapy	Comparators of interest are: • Other types of radiotherapy • Surgical resection • Other types of therapy for localized tumor	Relevant outcomes include: • Overall survival • Disease-free survival • Change in disease status • Treatment-related morbidity
Individuals: • With pediatric central nervous system tumor(s)	Interventions of interest are: • Charged-particle (proton or helium ion) radiotherapy	Comparators of interest are: • Other types of radiotherapy • Surgical resection • Other types of therapy for localized tumor	Relevant outcomes include: • Overall survival • Disease-free survival • Change in disease status • Treatment-related morbidity
Individuals: • With pediatric non-central nervous system tumor(s)	Interventions of interest are: • Charged-particle (proton or helium ion) radiotherapy	Comparators of interest are: • Other types of radiotherapy • Surgical resection • Other types of therapy for localized tumor	Relevant outcomes include: • Overall survival • Disease-free survival • Change in disease status • Treatment-related morbidity
Individuals: • With head and neck tumors other than skull-based	Interventions of interest are: • Charged-particle (proton or helium ion) radiotherapy	Comparators of interest are: • Other types of radiotherapy • Surgical resection • Other types of therapy for localized tumor	Relevant outcomes include: • Overall survival • Disease-free survival • Change in disease status • Treatment-related morbidity

Description

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.

Summary of Evidence

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) (i.e., 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 five-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 (e.g., intensity-modulated radiotherapy). The evidence is insufficient to determine the effects of the technology on health outcomes.

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 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

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.

Other applications of charged-particle irradiation with proton or helium ion beams are considered **investigational**. This includes, but is not limited to:

- pediatric non-central nervous system tumors,
- tumors of the head and neck (other than skull-based chordoma or chondrosarcoma).

Policy Guidelines

Evidence is unavailable to define age parameters for the use of proton beam therapy (PBT) in pediatric patients. Some studies using proton beam therapy in pediatric central nervous system (CNS) tumors mostly included patients younger than three years of age. However, experts cite the benefit of proton beam therapy in pediatric patients of all ages (less than 21 years of age).

Note: This protocol does not address radiation treatment for cancers of the prostate, breast, lung, colon and rectum, and including metastasis to the brain/spine or bone.

Medicare Advantage

Proton Beam Therapy (PBT) is considered **medically necessary** 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.

Medicare Advantage Policy Guidelines

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 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.

Group 2

Proton beam therapy in Group 2 is limited in that that medical necessity decisions must incorporate additional considerations of clinical scenario with appropriate documentation. Normal tissue dose volume histograms (DVHs) must be demonstrably improved with a PBT plan. The following disease sites/states may therefore be considered for the use of PBT utilizing the above medically necessary criteria in conjunction with the clinical scenario:

- Upper abdominal/peri-diaphragmatic cancers
- Advanced stage, unresectable pelvic tumors including those with peri-aortic nodes or malignant lesions of the cervix
- Unresectable pancreatic and adrenal tumors
- Skin cancer with macroscopic perineural/cranial nerve invasion of skull base
- Unresectable malignant lesions of the liver, biliary tract
- 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.

Background

Charged-particle beams consisting of protons or helium ions are a type of particulate radiotherapy (RT). They contrast with conventional electromagnetic (i.e., photon) RT due to several unique properties, including minimal scatter as particulate beams pass through tissue, and deposition of ionizing energy at precise depths (i.e., 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 two general categories of tumors and abnormalities:

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.

Advances in photon-based RT such as three-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, three to five fixed beams of protons or helium ions are used.

Regulatory Status

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 (including proton beam) are devices that require FDA oversight. Senior staff at the FDA's Center for Devices and Radiological Health have indicated that the proton beam facilities constructed in the United States prior to enactment of the 1976 Medical Device Amendments were cleared for use in the treatment of human diseases on a "grandfathered" basis, while at least one that was constructed subsequently received a 510(k) marketing clearance. There are 510(k) clearances for devices used for delivery of proton beam therapy and devices considered to be accessory to treatment delivery systems such as the Proton Therapy Multileaf Collimator (which was cleared in December 2009). Since 2001, several devices classified as medical charged-particle radiation therapy systems have received 510(k) marketing clearance. FDA Product Code LHN.

Related Protocols

Intensity-Modulated Radiotherapy: Abdomen and Pelvis

Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid

Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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