Molina Clinical Policy
Proton Beam Radiation Therapy: Policy No. 226

Last Approval: 6/9/2021
Next Review Due By: June 2022

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members.[1] References included were accurate at the time of policy approval and publication.

OVERVIEW [5-8,49]

Proton Beam radiotherapy (PBT) is a form of conformal external beam radiation treatment. Protons are positively charged atomic particles and have similar biological effects as conventional x-ray beams but have very different energy disposition or physics profiles. Proton particles deliver a smaller amount of radiation energy as they enter the body (lower entrance dose) culminating in an intensity dose peak (e.g. Bragg Peak) therefore depositing 100% of the dosage at the targeted tissue. There is no further energy deposition beyond the Bragg peak (no exit dose). Proton beams typically deposit less radiation in normal non-targeted tissues than conventional radiation therapy and have been used to escalate the radiation dose to diseased tissues while minimizing damage to adjacent normal tissues. Proton beam therapy will typically have a significantly lower integral dose (dose to the whole body of the patient) compared to conventional x-ray therapy. In contrast, conventional photon external beam radiation therapy (EBRT) delivers radiation to all tissue, diseased and normal, and targeted tissue receives 60–70% of the intended dose.

Proton beam therapy is typically performed on an outpatient basis. For most tumor sites, a standard course of treatment is five to seven weeks, with treatments delivered five days per week. The length of each treatment will vary depending upon the tumor type and stage. The delivery of the proton beam to the patient lasts only a few minutes, although the total time spent in the treatment room will be longer (about 15 to 20 minutes) for positioning and adjustments to the equipment settings.

COVERAGE POLICY [3-30,36,44-49]

Proton beam radiation therapy **may be considered medically necessary** and may be authorized for the following conditions when sparing the surrounding normal tissue cannot be adequately achieved with surgical excision, conventional photon beam radiation or Intensity-Modulated Radiation Therapy (IMRT).

1. As primary therapy for the following ocular tumors such as melanoma of the uveal tract (including the iris, choroid, or ciliary body tumors and Member meets **ALL** of the following:[3-9 10-16]
    - No evidence of metastasis or extrascleral extension; **AND**
    - Tumor size diameter ≤ 24 mm; **AND**
    - Tumor size height ≤ 14 mm.

OR

2. As postoperative therapy for the following head and neck skull base tumors: head and neck tumors that normal tissue dose constraints cannot be met with a photon-based plan (including the hypopharynx, nasopharynx, ethmoid sinus, salivary gland, mucosal melanoma, and advanced [e.g., T4] and/or unresectable head and neck cancers):[3-9 17-21]

    a. Chordoma at the base of the skull and **BOTH** of the following:
        - No distal metastasis; **AND**

- Residual localized tumor after resection.

OR

b. Chondrosarcoma at the base of the skull and **BOTH** of the following:
   - No distal metastases; **AND**
   - Grade I or II chrondrosarcoma; **AND**
   - Residual localized tumor after resection.

OR

3. For the following OTHER clinical conditions:[3-9 22-30 37-39]
   a. Arteriovenous Malformation (AVM) when **ONE** of the following is met:
      - Intracranial AVM not amenable to surgical excision or other conventional forms of treatment; **OR**
      - Adjacent to critical structures such as the optic nerve, brain stem or spinal cord.

   OR

   b. Cancers of the paranasal sinuses and other accessory sinuses; **OR**

   c. Central nervous system (CNS) lesions, primary or metastatic CNS malignancies (e.g., gliomas) when **BOTH** of the following are met:
      - Adjacent to critical structures such as the optic nerve, brain stem, or spinal cord; **AND**
      - Other standard radiation techniques such as IMRT or standard stereotactic modalities would not sufficiently reduce the risk of radiation damage to the critical structure.

   OR

   d. Nonmetastatic retroperitoneal sarcomas; **OR**

   e. Hepatocellular carcinoma when **BOTH** of the following are met:[4]
      - Intrahepatic tumor; **AND**
      - Patient is not candidate for or refuses surgery and ablation.

   OR

   f. Hodgkin lymphoma that normal tissue dose constraints cannot be met with a photon-based plan;[4] **OR**

   g. Non-Small Cell lung cancer;[4] **OR**

   h. Patients with genetic syndromes making total volume of radiation minimization crucial including Neurofibromatosis (NF-1) and retinoblastoma; **OR**

   i. Pituitary neoplasms; **OR**

   j. For Pediatric Members under age 21 who have **BOTH** of the following:
      - CNS tumors; **OR**
      - primary or benign solid tumors treated with curative intent.

   OR

   k. Repeat irradiation of previously treated fields where the dose tolerance of surrounding normal structures would be exceeded with 3D conformal radiation or IMRT.[3]

Limitations and Exclusions [4,31-35,40-43]

Proton beam therapy (PBT) is **considered not medically necessary** and may not be authorized for the treatment of the following conditions as clinical outcomes have not been shown to be superior to other approaches:

- Abdominal Tumors
- Age-Related Macular Degeneration (AMD)
- Breast Cancer
- Choroidal Hemangiomas
- Esophageal Cancer
- Ewing's and soft tissue sarcoma
- Gastric Cancer
- Pelvic Tumors (including genitourinary, gynecologic, and gastrointestinal)
- Pancreatic Cancer
- Prostate Cancer *Please reference *Proton Beam Therapy for prostate Cancer MCP-153*
- Thoracic Tumors
- Thymomas and Thymic Carcinoma
- Vestibular Tumors

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE [10-49]

Skull Base Tumors [17-21]

The published evidence consisting of systematic reviews, retrospective studies, and uncontrolled single arm studies is sufficient and supports that PBT is effective in the treatment of skull base tumors. A systematic review concluded that there is evidence for a benefit of proton beam therapy over photon approaches in treating chordomas. Another systematic review of seven uncontrolled single-arm studies concluded that the use of protons has shown better results in comparison to the use of conventional photon irradiation, resulting in the best long-term (10 years) outcome for skull-based chordomas with relatively few significant complications. A second systematic review by the same author reported that studies of proton beam therapy for skull-based chondrosarcoma resulted in local control ranging from 75% to 99% at 5 years. A retrospective review of 29 patients with skull base chordomas (n=18) and low-grade chondrosarcomas (CS) (n=11) assessed the clinical results of spot scanning proton beam radiation therapy (PT). Median follow-up time was 29 months (range, 6-68 months). Three year local control rates were 87.5% and 100% for chordoma and CS, respectively. According to this small study spot-scanning PT offers high tumor control rates of skull base chordoma and chondrosarcomas. A single center case series of 40 patients with chordomas of the skull base and cervical spine reviewed the outcomes of surgery and proton radiotherapy. The median follow-up was 56.5 months. The 5-year PFS and OS rates were 70% and 83.4%, respectively. Another single center case series evaluated the clinical results of fractionated spot-scanning proton radiation therapy (PT) in 26 pediatric patients treated at Paul Scherrer Institute for chordoma (CH) or chondrosarcoma (CS) of the skull base or axial skeleton. Mean follow-up was 46 months. Actuarial 5-year local control (LC) rates were 81% for CH and 80% for CS. Actuarial 5-year overall survival (OS) was 89% for CH and 75% for CS.

Uveal Melanomas [10-16]

The published evidence consisting of a RCT, comparative studies, retrospective cohort studies, and case series is sufficient and supports that PBT is effective in the treatment of uveal melanomas. A systematic review was conducted by the American Society for Therapeutic Radiology and Oncology (ASTRO) Evaluation Subcommittee of Emerging Technologies. The review noted that the use of PBRT has been reported in thousands of cases of ocular melanoma, with combined results of leading centers in the United States and Europe showing 95% control rate and 90% eye retention rate. The technique was noted as especially useful in large and posteriorly located melanomas

that are unapproachable by other techniques such as brachytherapy. This review concluded that there is evidence for a benefit of proton beam therapy over photon approaches in treating large ocular melanomas.

A report on proton beam therapy from the Institute for Clinical and Economic Review (ICER) rated the net health benefit of PBT relative to alternative treatments to be superior in ocular tumors. The RCT compared PBT alone to a combination of PBT and transpupillary thermotherapy (TTT) in 151 patients (mean age: 58 years; 52% male) treated for uveal melanoma and followed for a median of 3 years in France. Combination therapy was associated with a statistically-significantly (p=0.02) reduced likelihood of secondary enucleation; no other outcomes differed significantly between groups. In a separate comparison of these findings to a separate series of patients undergoing PBT with endoresection of the scar rates of secondary enucleation did not differ between groups, but rates of neovascular glaucoma were significantly lower in the PBT+endoresection group vs. the groups from the RCT (7% vs. 58% and 49% for PBT alone and PBT+TTT respectively, p<0.0001). Of note, however, median follow-up was less than two years in the PBT+endoresection series vs. 9 years in the RCT. Three of the cohort studies were all fair-quality and involved comparisons to surgical enucleation in patients with uveal melanoma at single centers. PBT was associated with statistically-significant improvements in overall survival rates relative to enucleation at 2-5 years in two of these studies. Rates of metastasis-related and all cancer-related death were statistically-significantly lower among PBT patients through two years of follow-up in the Seddon study, but were nonsignificant at later time points. The 5-year metastasis-free survival rate (n=67) was 50% higher among PBT patients in a Cox regression model controlling for baseline characteristics (59.0% vs. 39.4% for enucleation, p=0.02). In the third study, Kaplan-Meier curves for all-cause mortality, melanoma-related mortality and metastasis-free survival did not statistically differ for 132 patients treated with PBT and enucleation. Metastasis-free survival also did not differ in Cox regression adjusting for age, sex, and tumor thickness.

Another study assessed the impact of PBT + chemotherapy vs. PBT alone in 88 patients with uveal melanoma (aged primarily between 20-55 years; 63% male) who were followed for 5-8 years. Five-year overall survival rates did not statistically differ between groups on either an unadjusted or Cox regression-adjusted basis. Lastly, a comparison of non-contemporaneous case series evaluated treatment with PBT + laser photocoagulation or PBT alone in 56 patients with choroidal melanoma. At one year, there were no differences in visual acuity between groups.

Other Conditions [22-30-31-43]

According to the published peer reviewed literature, proton beam therapy (PBT) may be appropriate in circumstances where intensity modulated radiation therapy (IMRT) or stereotactic would potentially damage critical structures, particularly in patients with a history of prior irradiation. For pituitary gland tumors, proton therapy has distinct advantages in its ability to more precisely target tumor while shielding adjacent normal tissues. PBT is also appropriate for pediatric patients because even low doses of scattered radiation in this population can affect growth and development and increase the risk of secondary malignancies later in life. Results of proton therapy have been published for AVM and CNS lesions that have concluded that generally the use of PBT for these conditions is only medically appropriate in specific circumstances where adjacent critical structures cannot be adequately spared with surgery, IMRT or SRS. For other head and neck cancers and Hodgkin's lymphomas, the published evidence considers these conditions medically necessary when a photon-based plan cannot safely deliver the desired dose of radiation.[4,24-30,44-48]

There is limited clinical evidence that directly compares proton beam therapy (PBT) with other types of radiation therapy for other conditions. The current published evidence is of low quality and consists of small comparative studies that are not randomized or controlled, retrospective/prospective studies and individual case series. There is very limited published data in the peer reviewed literature regarding the use of PBT for breast cancer, other GI cancers, and any other condition not listed above. Therefore, the current published evidence does not allow for any definitive conclusions about the safety and efficacy of proton beam therapy to treat other conditions not listed in the medically necessary recommendation section above.[31-43]

Professional Society Guidelines

The **American Society for Radiation Oncology (ASTRO)** issued a 2017 update to its recommendations for the use of proton beam therapy to treat cancer. The updated model policy outlines appropriate clinical indications, or diagnoses, for proton beam therapy that include the following:[6]

- Malignant and benign primary central nervous system (CNS) tumors
- Advanced (e.g., T4) and/or unresectable head and neck cancers
- Cancers of the paranasal sinuses and other accessory sinuses
- Nonmetastatic retroperitoneal sarcomas
- Reirradiation cases where cumulative critical structure dose would exceed tolerance dose
- Hepatocellular cancer
- Ocular tumors, including intraocular melanomas
- Tumors that approach or are located at the base of skull, including but not limited to chordoma and 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
- Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors when one of the 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

SUPPLEMENTAL INFORMATION

None.

CODING & BILLING INFORMATION

CPT Codes

CPT	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 Code

HCPCS	Description
S38030	Scleral application of tantalum ring(s) for localization of lesions for proton beam therapy

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/9/2021	Policy reviewed, updated criteria based on recommendations considered appropriate from NCCN and other guidelines. Added HCC cancer and non-small lung cancer as medically necessary; added Ewing's and soft tissue sarcoma, and Thymomas and Thymic Carcinoma to not medically necessary. Updated references.
4/23/2020	Policy reviewed, no changes.
3/11/2019	Policy reviewed and updated based on new evidence-based literature. Updated ACR-ASTRO and NCCN guidelines. Pituitary gland tumors, Hodgkin's lymphomas and other head and neck cancers added as medically necessary.
7/10/2018	Policy reviewed and updated based on new evidence-based literature. Updated ASTRO and NCCN guidelines. Added as medically necessary: AVM, cancers of the paranasal sinus, CNS tumors, nonmetastatic retroperitoneal sarcomas, genetic syndromes such as retinoblastoma and neurofibromatosis (NF-1), pediatric CNS and solid tumors and repeat irradiation of previously treated fields. Summary of Medical Evidence and references updated.
12/16/2015, 9/15/2016, 6/22/2017	No changes.
3/25/2015	New policy.

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National and Specialty Organizations

3. AIM Specialty Health. Clinical appropriateness guidelines: Radiation oncology, proton beam therapy guidelines. Published 2021. https://aimspecialtyhealth.com/resources/clinical-guidelines/radiation-oncology/.
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   - Bone Cancer, Breast Cancer, Central Nervous System Cancers, Esophageal and Esophagogastric Junction Cancers, Head & Neck Cancers, Hodgkins Lymphoma, Hepatobiliary Cancers, Non-Small Cell Lung Cancer, Soft Tissue Sarcoma, Thymomas and Thymic Carcinomas, Uveal Melanoma
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    - Proton beam therapy for treatment of chordoma and chondrosarcoma of the skull base. Published Dec 2019. Updated Feb 2021.
    - Proton beam therapy for non-small cell lung cancer. Published January 2017. Updated February 2021.
    - Proton beam therapy for treatment of pituitary adenomas. Published February 2019. Updated March 2021.
    - Proton beam therapy for treatment of head and neck cancer. Published October 2019. Updated February 2021.
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54. MCG Health. Ambulatory care: Procedures and diagnostic tests, hematology-oncology, proton beam therapy (A-0389).

APPENDIX

Reserved for State specific information *(to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*