MEDICAL POLICY

MEDICAL POLICY DETAILS	
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Product Disclaimer	• *Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *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.* • *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.* • *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 (PBT) has been medically proven to be effective and therefore, is considered **medically appropriate** for the curative treatment of **ANY** of the following indications when criteria are met:
   A. Cancers of the Head and Neck including:
      1. Ocular tumors, including intraocular (Uveal) melanomas;
      2. Peri-ocular tumors invading the orbit, skull base, or cavernous sinus;
      3. Nasopharynx, nasal cavity, paranasal sinuses and other accessory sinuses;
      4. Unresected T3, T4, or node positive head and neck cancers;
   B. Central Nervous System Cancers including:
      1. Curative treatment of primary central nervous system tumors or malignancies requiring cranial or craniospinal irradiation (e.g., medulloblastoma, gliomas, primary spinal cord tumors);
   C. Abdominal Cancers including:
      1. Localized unresectable hepatocellular carcinoma or intrahepatic cholangiocarcinoma when any of the following criteria are met:
         a. When a single lesion is present, the lesion must be 15cm or greater in greatest dimension;
         b. When two lesions are present, one lesions is greater than 10cm in greatest dimension;
         c. When three lesions are present, one lesion is greater than 6cm in greatest dimension;
      2. Non-metastatic retroperitoneal sarcomas;
   D. Thoracic Tumors including any of the following:
      1. Primary tumors of the mediastinum (i.e., thymoma and thymic tumors, mediastinal tumors, mediastinal lymphomas and thoracic sarcomas);
      2. Malignant pleural mesothelioma;

E. Stage IIA pure testicular seminoma;
F. Pediatric Cancers including any of the following:
   1. Central nervous system tumors;
   2. Other pediatric malignancies if consultation with a radiation oncologist determines an increased predicted risk of radiation-induced late effects;
G. Primary malignant or benign bone tumors (e.g.; Chordomas, chondrosarcomas, osteosarcoma or Ewing sarcoma when localized and in the postoperative setting;
H. Genetic syndromes including any of the following:
   1. Neurofibromatosis type 1 (NF-1);
   2. Li-Fraumeni;
   3. Ataxia Telangiectasia (with deleterious ATM mutations);
   4. Hereditary Retinoblastoma;
   5. Lynch syndrome; or
   6. Hereditary Breast or Ovarian Cancer (with BRCA 1 and BRCA 2 mutations);
I. Re-irradiation with curative intent where cumulative critical structure dose will exceed tolerance dose;
J. Individuals with a single kidney or transplanted pelvic kidney with treatment of an adjacent target volume.

II. Based upon our criteria and assessment of the peer reviewed literature, charged particle irradiation with PBT has not been medically proven to be more effective than other highly-focal techniques (e.g., intensity-modulated radiation therapy [IMRT]) 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 #6.01.24 Intensity Modulated Radiation Therapy

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Refer to Corporate Medical Policy #11.01.13 Out-of-Network Services

POLICY GUIDELINE

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 National Association of Proton Centers website for more information: https://www.proton-therapy.org/map/ accessed 07/30/24.

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. Protons have a unique property known as the Bragg peak. The Bragg peak is the depth dose distribution exhibited by the particles. When the positively charged atomic particles 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 and then stop. Beyond the Bragg peak, protons have a 5mm dose deposition. 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 has a slower delivery speed than photon therapy, and requires specialized equipment in the form of accelerators (cyclotrons, synchrotrons, synchrocyclotrons, or linear accelerators)

PBT Treatment Planning consists of:

I. Simulation and imaging using CT, CT/PET, and or MRI;
II. Contouring, which defines the target volume and structures to be avoided;
III. Radiation dose prescription;
IV. Dosimetric planning and calculations;
V. Patient specific dose verification.

Per the American Society of Radiation Oncology (ASTRO) Model Policy for Proton Beam Therapy (2022) PBT may be considered reasonable when:

I. "The target volume is near 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), which would portend a higher risk of toxicity.

II. A proton-based technique would decrease the probability of clinically meaningful normal tissue toxicity by lowering an integral dose-based metric and/or organ at risk dose volume constraints associated with toxicity.

III. 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."

Additionally, ASTRO recommends that the radiation oncologist conduct an informed assessment of the benefits and risks including:

A. Determination of patient suitability for PBT allowing for reproducible treatment delivery;
B. Adequate definition of the target volumes and organs at risk;
C. Equipment capability, including ability to account for organ motion when relevant;
D. Physician, physicist and staff training;
E. Adequate quality assurance and safety procedures.

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.

Cancers of the Head and Neck

Primary Ocular Tumors Including Intraocular/Uveal Melanomas

Uveal melanoma, although rare, is the most common primary intraocular malignancy in adults. Management is individualized and must consider tumor size, location, extension or metastases, potential disruption to vision, as well as patient preferences. It is highly radioresistant, and requires high-dose radiation, most commonly, plaque brachytherapy.

Previously, charged particle beam therapy (e.g., PBT) was felt to have lower recurrence rates when compared to brachytherapy, but the use of radiosonography in the intraoperative setting has allowed for plaque localization, and has decreased the rate of recurrence, demonstrating that charged particle beam therapy and brachytherapy are equally as effective. Charged particle beam therapy has been associated with anterior eye complications, including damage to adjacent ocular structures such as the optic nerve, retina, lens, cornea and iris, and is therefore best utilized for patients who are not candidates for brachytherapy (e.g., gross extension within the orbit, no light perception).

The National Comprehensive Cancer Network (NCCN) Version 1.2024 Guidelines for Melanoma-Uveal: principles of radiation therapy, state that particle beam [utilizing protons] therapy is appropriate as upfront therapy after initial diagnosis, after margin-positive enucleation, or for intraocular or orbital recurrence. NCCN provides dosing of 50-70 cobalt Gray equivalent (CGyE) in 4-5 fractions to encompass the planning target volume surrounding the tumor.

A 2012 systematic review by Wang and colleagues reviewed 27 studies representing 8809 uveal melanoma patients to evaluate the efficacy and adverse effects of charged particle therapy. The rate of local recurrence was significantly less with charged particle therapy, than with brachytherapy. There was no significant difference identified in mortality or enucleation rates. Charged particle therapy was also associated with lower retinopathy and cataract formation rates.

Peri-ocular Tumors Invading the Orbit, Skull Base, or Cavernous Sinus

The National Comprehensive Cancer Network (NCCN) Version 4.2024 Guidelines for head and neck cancers states that "highly conformal dose distribution is important for patients whose primary tumors are located in the periocular area or invade the orbit, skull base, and/or cavernous sinus; extend intracranially or exhibit extensive perineural invasion; and

who are being treated with curative intent and/or who have long life expectancies" following treatment. PBT may have the ability to spare important organs at risk, decreasing the risk for late-onset toxicities.

A systematic review and meta-analysis by Palavani et al. 2024 evaluated the efficacy and safety of different radiotherapy modalities for skull base chordoma. A total of 32 studies were included, comprising 2322 patients who were treated with radiotherapy. The 5-year overall survival findings were as follows: in photon fractionated radiotherapy, an estimated rate of 77% (69%–84%, 568 patients); in conventional fractionated radiotherapy, 76% (65%–87%, 517 cases); and in proton-based + carbon ion–based radiotherapy, 85% (82%–88%, 622 cases). The 5-year progression free survival estimate rates were as follows: 35% (26%–45%, 95 cases) for photon fractionated therapy; 35% (25%–45%, 85 cases) for stereotactic radiotherapy; 77% (50%–100%, 180 cases) for proton-based and carbon ion–based radiotherapy; and 74% (45%–100%, 102 cases) for proton-based radiotherapy. Estimated rates of local control in periods of 3 and 5 years after proton- and carbon ion–based therapy were 84% (78%–90%, 326 cases) and 75% (65%–85%, 448 cases), respectively. For proton-based radiotherapy and carbon ion–based therapy, the 5-year local control rates were 76% (67%–86%, 259 cases) and 75% (59%–91%, 189 cases), respectively. The authors concluded that particle-based modalities like proton beam and carbon ion are the most effective radiation therapies available for the treatment of skull based chordoma.

Nasopharynx, Nasal Cavity, Paranasal Sinuses and Other Accessory Sinuses

NCCN V 4.2024 states "Proton therapy has typically been used to treat patients with the most challenging disease configurations, for which other [radiation therapy] options were not felt to be safe or of any benefit. In cancers of the oropharynx, supraglottic larynx, nasopharynx, paranasal sinus, and salivary glands, as well as mucosal melanoma, and unknown primary tumors of the head and neck, the panel agrees that proton therapy should be considered when normal tissue constraints cannot be met by photon-based therapy, or when photon-based therapy causes compromise of standard radiation dosing to tumor or postoperative volumes. The panel supports ongoing efforts to develop models to predict which patients would benefit the most from proton therapy and the development of higher-level and/or randomized data demonstrating greater efficacy or meaningful [quality of life] gains potentially achieved with PBT."

Central Nervous System Cancers

The NCCN V1.2024 Clinical Practice Guidelines in Oncology for central nervous system cancers states, in efforts to diminish the dose to critical structures, proton therapy can be considered for the following malignancies requiring craniospinal radiation therapy: intracranial and spinal ependymoma, leptomeningeal metastases, high-grade glioma (isocitrate dehydrogenase (IDH)-mutant and 1p19q codeleted tumors), re-irradiation of gliomas when clinical trial options and new systemic therapy options are limited, primary spinal cord tumors, and meningiomas.

In regard to the reirradiation of gliomas, NCCN states, "Recurrence of glioma can be managed with reirradiation in select scenarios when clinical trial options and new systemic therapy options are limited. Target volumes will be defined using contrast-enhanced CT and/or MRI images. Normal tissues should include the brain, brainstem, optic nerves, and chiasm. Radiation dose should be optimized and conformed to the target volume, while diminishing dose to critical structures. Treatment may be performed with highly focused modern SRS techniques for lower volume disease; fractionated IMRT, including doses of 35 Gy in ten fractions for recurrent glioblastoma, and proton therapy to help spare previously irradiated normal brain."

Abdominal Cancers

Hepatocellular Carcinoma and Intrahepatic Biliary Cancers

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.

Non-metastatic Retroperitoneal Sarcomas

In 2017, Delaney and colleagues conducted a Phase 1 trial comparing preoperative photon IMRT with intensity modulated PBT in 11 patients with primary or locally recurrent retroperitoneal sarcoma to determine the maximum tolerated dose to clinical target volume. All patients were treated with 50.4 GyRBE in 28 fractions to CTV1 (gross tumor volume and adjacent tissues at risk of subclinical disease) with a simultaneous integrated boost to CTV2 (radiation dose to tumor volume) to doses of 60.2, 61.6, and 63.0 GyRBE in 28 fractions of 2.15, 2.20 and 2.25 GyRBE. All patients were able to achieve dose escalation to maximum tolerated dose without acute dose limiting toxicities, and with no perioperative morbidity noted during the 18-month median follow up.

NCCN V1.2024 guidelines for soft tissue sarcoma states that radiation therapy can be administered as either neoadjuvant treatment for patients with resectable disease or as a primary treatment for those with unresectable disease and emphasizes that radiation is not a substitute for definitive surgical resection. The guidelines state that newer radiation techniques such as IMRT and protons may allow tumor target coverage and acceptable clinical outcomes within normal tissue dose constraints to organs at risk.

Thoracic Tumors

Thymoma or Thymic Carcinoma

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 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 IMRT while adjuvantly treating thymomas in 4 patients at a single proton therapy center.

The NCCN V1.2024 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.

Malignant Pleural Mesothelioma(MPM)

Mesothelioma is a rare malignancy with a poor prognosis. Treatment options are determined by factoring the extent of the disease, performance status, baseline pulmonary function and tumor histology. The definition of optimal management is undecided, with several options of treatment having significant risks of toxicity, including radiation, and therefore, intensity modulated radiation therapy (IMRT) has not been recommended. Small institutional studies of treatment with proton beam have demonstrated improvements in target coverage and reduced mean radiation doses to the kidneys, contralateral lung, heart, spinal cord and liver, and in some cases, by half.

In 2019, the National Cancer Institute’s Thoracic Malignancy Steering Committee, along with the International Association for the Study of Lung Cancer and Mesothelioma Applied Research Foundation, published a summary of expert opinion on the use of radiation therapy for the treatment of MPM (Gomez, et al 2019). The committee acknowledged that “clinical outcomes data for proton therapy in the setting of MPM are sparse, several dosimetric studies have demonstrated that intensity-modulated proton therapy provides superior sparing of normal tissue of the ipsilateral and contralateral kidneys, liver, heart, esophagus, and contralateral lung than is possible with IMRT after extrapleural pneumonectomy, while also significantly improving planning target volume (PTV) coverage.” The committee based their

opinion on both the dosimetric studies and results from prospective studies and large series conducted on patients with locally advanced non-small cell lung cancer, small cell lung cancer and thymic malignancies, treated with PTB.

The Particle Therapy Cooperative Group's thoracic subcommittee published a consensus statement (Zeng, et al 2020) for the use of proton therapy in mesothelioma treatment stating, "For patients receiving nonpalliative radiation therapy for mesothelioma, proton therapy is likely to be beneficial in terms of its ability to decrease radiation dose to the contralateral lung (the greatest potentially life-threatening toxicity risk in radiation therapy for mesothelioma), and other organs such as heart, liver, and kidneys. Proton therapy has clear dosimetric advantages over photon therapy." The subcommittee acknowledged that the current literature is promising and the current poor prognosis for patients with mesothelioma requires strategies to increase the effectiveness of treatment, to decrease toxicity, and to improve quality of life.

NCCN V1.2024 guidelines for pleural mesothelioma states that, "Advanced technologies are appropriate when needed to deliver curative [radiation therapy] safely. These technologies include (but are not limited to) 4D-CT and/or PET/CT simulation, IMRT/volumetric modulated arc therapy (VMAT), IGRT, motion management, and proton therapy. Special attention should be paid to minimize radiation to the contralateral lung, as the risk of fatal pneumonitis with IMRT is excessively high when strict limits are not applied."

Stage IIA Pure Testicular Seminoma

Germ cell tumors (pure seminoma and nonseminomatous) account for 95% of testicular cancers. Stage I seminoma is typically treated with orchiectomy and has good outcomes in disease-free survival. Individuals with prognostic Stage II Testicular Cancer Seminoma are defined as having pure seminoma and disease spread to the lymph nodes. These individuals are typically treated with radiation therapy and/or chemotherapy and studies of overall survival comparing the two have reported different outcomes. Retrospective studies (Glaser et al, 2016, Paly et al. 2016) have assessed the five year overall survival of patients receiving radiation therapy vs. chemotherapy in Stage IIA and IIB Seminoma. The studies demonstrated that overall survival was significantly higher for individuals with IIA seminoma receiving radiation therapy vs. chemotherapy but there was no significant difference for those with stage IIB seminoma. NCCN, in theV.1.2024 Guidelines for Testicular Cancer recommends either radiation therapy or chemotherapy for both IIA and IIB Seminoma, which can include PBT, but that radiation should be "reserved for select patients with non-bulky (≤3cm) disease. It should be noted that IIB Seminoma, as defined by the American Joint Committee on Cancer (AJCC) TNM Staging Classification for Testis Cancer (2017) incorporates multiple lymph nodes, with any one mass larger than 2cm but not larger than 5cm in greatest dimension.

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 twenty 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.

NCCN V1. 2025 guidelines for adolescent and young adult oncology identifies that radiation therapy is associated with increased risks of delayed morbidity and mortality; development of secondary malignant neoplasms, as well as pulmonary, cardiac, thyroid dysfunction, chronic health conditions and growth abnormalities. Given such, for patients with a predicted risk of radiation-induced late effects to tissues surrounding but not in targeted conditions, consultation with a radiation oncologist for proton radiotherapy should be considered.

Primary Malignant or Benign Bone Tumors

Chordomas and Chondrosarcomas

Chordomas and chondrosarcomas are rare malignant neoplasms of the bone. Chordomas arise from the notochord and present at the base of the skull (sphenooccipital region) for one third of the adults diagnosed. Chondrosarcomas come

from the middle fossa, posterior, or anterior fossae and account for six percent of all skull base tumors. Skull base tumors are most often found adjacent to critical structures and are primarily treated with surgery and postoperative radiation therapy. Literature supporting the use of PBT in these tumors is limited. There are no randomized trials to date supporting the use of PBT over conventional treatments, however given the need to spare surrounding tissues within the central nervous system, its use is considered medically necessary in the post-operative setting.

NCCN V2.2024 Bone Cancer guidelines principles of radiation therapy recommends considering specialized techniques such as IMRT, particle beam radiation therapy with protons, carbon ions, or other heavy ions in order to allow high-dose therapy while maximizing normal tissue sparing. Further, that PTB used alone or in combination with photon beam radiation therapy has been associated with an excellent local tumor control and long-term survival in the treatment of patients with low-grade skull base and cervical spine chondrosarcomas.

Genetic Syndromes

Any disruption in the integrity of a cell's DNA can cause uncontrolled growth and division. DNA is constantly damaged through environmental factors. Cells contain repair mechanisms in order to help the body compensate. Radiation therapy causes the accumulation of DNA damage. Radiation doses to the tumor target are very high, with distant organs receiving low to moderate doses as bystanders as a result. How an individual's DNA repair mechanisms respond to radiation therapy is variable and is in part determined by age and genetic factors.

Several genetic syndromes have been correlated with radiosensitivity, where DNA damage occurs and is left unrepaired. This type of damage causes adverse tissue events that are attributable to the death of the cells. The most radiosensitive syndrome is Ataxia Telangiectasia (homozygous ATM mutations).

Other genetic mutations have been correlated with radiosusceptibility, which includes misrepaired DNA damage, cell transformation and genomic instability. This damage causes a predisposition to radiation-induced cancers. Examples of genetic syndromes correlated with radiosusceptibility include Neurofibromatosis type 1 (NF-1), Li Fraumeni syndrome (germline variants in TP53), hereditary retinoblastoma, lynch syndrome, hereditary breast and ovarian cancer with BRCA 1 or BRCA 2 mutations.

Thariat, et al. 2021 explore the management of patients with Li-Fraumeni or heritable TP53-related cancer syndromes based on their susceptibility to radiation and provide guidelines for avoiding or adapting radiotherapy when able, stating that radiotherapy of all types should be avoided when non-genotoxic curative techniques, such as surgery, are available. In situations where radiotherapy cannot be avoided, as is the case for individuals with advanced breast cancer who have a high probability of locoregional relapse, and heritable TP53-related cancer syndromes, hadrontherapy (proton therapy in particular) might be preferred to limit irradiated volumes.

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).

NCCN guidelines V4.2024 for prostate cancer acknowledge that photon and proton are both forms of external beam radiation therapy that appear to have generally comparable biochemical control and that the cost of proton beam therapy was more than double the cost of IMRT and SBRT. Further, ASTRO (included within the 2022 Model Policy) states that there is a need for continued clinical evidence development and comparative effectiveness analysis for the appropriate use

and that PTB for the treatment of prostate cancer should occur in the setting of a clinical trial or multi-institution patient registry.

ASTRO's 2022 model policy states that PBT is considered reasonable in instances where sparing the surrounding normal tissue cannot be achieved with photon-based radiotherapy and is of added clinical benefit to the patient. The policy lists three scenarios of when PBT might be preferred over conventional radiotherapy, including when the target volume is near 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), which would portend a higher risk of toxicity, a proton-based technique would decrease the probability of clinically meaningful normal tissue toxicity by lowering an integral dose-based metric and/or organ at risk dose volume constraints associated with toxicity, and 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.

On the basis of the medical necessity requirements and published clinical data, disease sites that frequently support the use of PBT include the following:

I. Benign or malignant tumors or hematologic malignancies in children aged 21 years and younger treated with curative intent and occasionally palliative intent when at least one of the three primary criteria apply;
II. Benign or malignant tumors or hematologic malignancies in the adolescent/young adult population aged 22 to 39 years treated with curative intent when at least one of the three primary criteria apply;
III. Patients with genetic syndromes making the total volume of radiation minimization crucial (e.g., NF-1, deleterious ATM mutations, Li-Fraumeni, retinoblastoma;
IV. Patients with genetic syndromes at risk of developing second cancers at or near the same body location (e.g., BRCA1, BRCA2, Lynch syndrome;
V. Patients who are not surgical candidates;
VI. Re-irradiation;
VII. Primary malignant of benign bone tumors;
VIII. Ocular tumors, including intraocular melanomas;
IX. Tumors that approach or are located at the base of the skull (e.g., chordoma, chondrosarcomas);
X. Malignant and benign primary CNS tumors excluding IDH wild-type glioblastoma treated with curative intent and with potential for long term prognosis;
XI. 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);
XII. Primary and metastatic tumors requiring craniospinal irradiation;
XIII. Cancers of the nasopharynx, nasal cavity, paranasal sinuses, and other accessory sinuses,
XIV. Advanced stage unresectable head and neck cancers
XV. Primary cancers of the esophagus;
XVI. Primary tumors of the mediastinum, including thymic tumors, mediastinal tumors, mediastinal lymphomas and thoracic sarcomas;
XVII. Malignant pleural mesothelioma;
XVIII. Primary hepatocellular cancer and intra-hepatic biliary cancers;
XIX. Advanced and unresectable pelvic tumors with significant pelvic and/or peri-aortic nodal disease;
XX. Patients with a single kidney or transplanted pelvic kidney with treatment of an adjacent target volume and in whom maximal avoidance of the organ is critical.

PBT would be considered as part of "coverage with evidence development" (CED) and only for those individuals enrolled in either an IRB-approved clinical trial or in a multi-institutional patient registry adhering to Medicare requirements for CED for indications that include, but not limited to the following: Cutaneous tumors with cranial nerve invasion to the base of skull, cavernous sinus and/or brainstem, head and neck cancers requiring ipsilateral radiation treatment (e.g., oral cavity, salivary gland), mucosal melanoma, breast cancer patients with unfavorable anatomy, end stage left sided breast cancer, patients with involved or suspicious internal mammary lymph nodes, early stage lung cancer, locally advanced lung cancer, kidney and

adrenal cancers, oligometastatic liver lesions, prostate cancer, non-metastatic rectal, bladder and cervical cancers.

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.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

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
C00.0-C14.8	Malignant neoplasm of head and neck sites (code range)
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)
C33.0	Malignant neoplasm of trachea
C38.0-C38.8	Malignant neoplasm of heart, mediastinum and pleura (code range)
C40.0-C40.8	Malignant neoplasm of bone and articular cartilage (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)
C45.0	Mesothelioma
C48.0-C48.8	Malignant neoplasm of retroperitoneum and peritoneum (code range)
C61	Malignant neoplasm of prostate
C69.00-C69.82	Malignant neoplasm of ocular structures (code range)

Code	Description
C70.0-C72.59	Malignant neoplasm of meninges, brain, cranial, nerves, spinal cord, and other parts of central nervous system (code range)
C75.1-C75.5	Malignant neoplasm of pituitary gland, craniopharyngeal duct, pineal gland, carotid body, aortic body and other paraganglia
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)
C81.02	Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.72	Other Hodgkin lymphoma, intrathoracic lymph nodes
C82.32	Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.72	Burkitt lymphoma, intrathoracic lymph nodes
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
D02.3	Carcinoma in situ of other parts of respiratory system
D07.5	Carcinoma in situ of prostate
D16.0-D16.8	Benign neoplasm of bone (code range)
D32.0-D33.7	Benign neoplasm of meninges, brain and other parts of central nervous system (code range)
D35.3	Benign neoplasm of craniopharyngeal duct
Z92.3	Personal history of irradiation

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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, hadrontherapy.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination (LCD#L35075) 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&] accessed 07/08/24.