Clinical Policy: Proton and Neutron Beam Therapies

Reference Number: CP.MP.70 Coding Implications
Date of Last Revision: 11/25 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Proton beam therapy (PBT) is a form of external beam radiation therapy (EBRT) that utilizes protons (positively charged subatomic particles) to precisely target a specific tissue mass. Proton beams can penetrate deep into tissues to reach tumors, while delivering less radiation to surrounding tissues. This may make PBT more effective for inoperable tumors, or for those areas in which damage to healthy tissue would pose an unacceptable risk.

Neutron beam therapy (NBT) is a less widely available form of EBRT that utilizes neutrons. Its clinical use is very limited due to difficulties in the delivery of this treatment modality.

Policy/Criteria
I. It is the policy of health plans affiliated with Centene Corporation® that proton beam therapy (PBT) is **medically necessary** for the following indications:
A. Ocular tumors, including but not limited to, intraocular melanomas;
B. Primary spine or spinal cord tumors or metastatic tumors of the spine or spinal cord for which organ-at-risk tolerance may be exceeded with photon treatments;
C. Tumors that approach or are located at the base of the skull, including but not limited to, chordoma or chondrosarcoma;
D. Hepatocellular cancer and intra-hepatic biliary cancers;
E. Primary or benign solid tumors or other hematologic malignancies in members/enrollees ≤ 21 years old;
F. Tumors/cancers that can be treated with any other type of radiation in members/enrollees with a known genetic mutation/syndrome increasing the risk of cancer;
G. Malignant and benign primary CNS tumors, excluding IDH wild-type glioblastoma (GBM);
H. Pituitary neoplasms;
I. Advanced staged and unresectable head and neck cancers;
J. Cancers of the nasopharynx, nasal cavity, paranasal sinuses and other accessory sinuses, when normal tissue constraints cannot be met by photon-based therapy;
K. Non-metastatic retroperitoneal sarcomas;
L. Re-irradiation cases where cumulative critical structure dose would exceed tolerance dose;
M. Primary tumors of the mediastinum, including thymic tumors (i.e. thymoma, thymic carcinoma), mediastinal tumors and mediastinal lymphomas (i.e. Hodgkin lymphoma and Non-Hodgkin lymphoma), and thoracic sarcomas;
N. Non-small cell lung cancer, to spare critical structures when critical organ dose constraints cannot be met with photon therapy (including three dimensional and IMRT neutron techniques);
O. Malignant pleural mesothelioma;
P. Primary malignant or benign bone tumors;

Q. Medically inoperable patients with a diagnosis of cancer typically treated with surgery where dose escalation is required due to the inability to receive surgery;
R. Primary and metastatic tumors requiring craniospinal irradiation;
S. Primary cancers of the esophagus;
T. Advanced and unresectable pelvic tumors with significant pelvic and/or peri-aortic nodal disease;
U. Members/enrollees 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.
V. Salivary gland tumors;
W. Arteriovenous malformations (AVM).

II. It is the policy of health plans affiliated with Centene Corporation that neutron beam therapy (NBT) **is medically necessary** in the treatment of salivary gland tumors when meeting any of the following:
A. The tumor is considered surgically unresectable, recurrent, or is resected with gross residual disease or positive margins;
B. Member/enrollee is medically inoperable.

III. It is the policy of health plans affiliated with Centene Corporation that all other indications for PBT and NBT are considered **not medically necessary** as insufficient evidence exists to recommend proton and/or neutron beam therapy as superior to other treatments available.

Background

Proton beam therapy (PBT) is an important method of treatment used in managing malignant disease with a well-defined target. Unlike x-rays, protons cause little damage to the tissues they pass through to reach their destination. Their energy is released after traveling a specified distance, thus delivering more radiation to the tumor and doing less damage to the nearby normal tissue. Because of this, PBT may be more useful for tumors with distinct edges rather than those whose edges are mixed with normal tissue.

Radiation therapy (RT) plays a critical role in the local tumor control of benign and low-grade central nervous system tumors in children but is not without the risk of long-term treatment-related sequelae. PBT is an advanced RT modality with a unique dose-deposition pattern that allows for treatment of a target volume with reduced scatter dose delivered to normal tissues compared with conventional photon RT and is now increasingly utilized in children with the hope of mitigating radiation-induced late effects.[1]

The American Society of Radiation Oncology (ASTRO) evaluated the evidence of use of PBT and listed examples of indications for coverage of PBT in their 2023 Model Policy for PBT, which includes, but is not limited to the following:

1. 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.
2. 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 constraint associated with toxicity.

3. 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.[2(p.3)]

ASTRO states there is a need for continued clinical evidence development and comparative effectiveness analyses for the appropriate use of PBT for various disease sites and as such all other indications are suitable for Coverage with Evidence Development (CED). They note that radiation therapy for patients treated under the CED paradigm should be covered by the insurance carrier as long as the patient is enrolled either in an IRB-approved clinical trial or in a multi-institutional patient registry adhering to Medicare requirements for CED.[2]

Head and Neck Cancer

Guidelines from National Comprehensive Cancer Network (NCCN) regarding PBT in the treatment of head and neck cancer state the following. "Achieving highly conformal dose distributions is especially important for patients whose primary tumors are periocular in location and/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. Non-randomized single institution clinical reports and systematic comparisons demonstrate safety and efficacy of PBT in the above-mentioned specific clinical scenarios. Proton therapy can be considered when normal tissue constraints cannot be met by photon-based therapies, or when photon-based therapy causes compromise of standard radiation dosing to tumor or postoperative volumes."[3(p2)]

Central Nervous System Cancers

NCCN guidelines note that it is reasonable to consider proton beam therapy for craniospinal irradiation where available, as it is associated with less toxicity.[4]

Uveal Melanoma

Per NCCN guidelines on uveal melanoma, "Tumor localization for proton beam therapy may be performed using indirect ophthalmoscopy, transillumination, and/or ultrasound (intraoperative or postoperative but before proton beam), x-ray, MRI and/or CT."[5(p2)]

A practice parameter on PBT from the American College of Radiology/ASTRO also notes that "commonly, the ophthalmologist will guide patient selection with tumor/target definition through techniques such as funduscopic examination, fluorescein angiogram, ultrasound, and direct tumor measurements intraoperatively. Most commonly but not imperatively, radio-opaque fiducial markers are sutured to the sclera and used as references for tumor definition. Treatment planning for ocular tumors has been most frequently performed with a treatment planning algorithm and software system developed specifically for treatment of ocular tumors. Other alternative approaches have been devised when special eye line is not available."[6]

Non-metastatic Retroperitoneal Sarcomas

Per NCCN guidelines on soft tissue sarcoma (STS), surgical resection of a localized tumor with negative margins is the standard, potentially curative treatment for patients with retroperitoneal/intra-abdominal STS. Radiation therapy (RT) can be administered as preoperative treatment for patients with resectable disease or as a primary treatment for those with

unresectable disease. Post-operative RT is discouraged but may be considered in rare instances. Newer RT techniques such as IMRT and 3D conformal RT using protons or photons may allow tumor target coverage and acceptable clinical outcomes within normal tissue dose constraints to adjacent organs at risk. When EBRT is used, sophisticated treatment planning with IMRT, tomotherapy and/or proton therapy can be used to improve therapeutic effect. However, the safety and efficacy of adjuvant RT techniques have yet to be evaluated in a multicenter RCT. RT is not a substitute to definitive surgical resection with negative margins, and re-resection to negative margins is preferable.[7]

Hepatocellular Cancer

Per NCCN guidelines on hepatocellular carcinoma (HCC), EBRT is a treatment option for patients with unresectable disease, or for those who are medically inoperable due to comorbidity. All tumors irrespective of the location may be amenable to RT [3D conformal RT, IMRT, and stereotactic Body Radiation therapy (SBRT)]. Image-guided radiotherapy is strongly recommended when using EBRT, IMRT, and SBRT to improve treatment accuracy and reduce treatment-related toxicity. Hypofractionation with photons or protons is an acceptable option for intrahepatic tumors, though treatment at centers with experience is recommended. PBT may be appropriate in specific situations.[8] In a phase II study, 94.8% of patients with unresectable HCC who received high dose hypofractionated PBT demonstrated >80% local control after two years, as defined by RECIST criteria.[9] Several ongoing studies are continuing to investigate the impact of hypofractionated PBT on HCC outcomes, including randomized trials comparing PBT to radiofrequency ablation (RFA). Data has demonstrated that local control is exceptional regardless of the fractionation used.[10] In a phase III study using the Child-Pugh classification, an evaluation of clinical outcomes of PBT versus RFA demonstrated PBT could be applied safely in patients with small recurrent hepatocellular carcinoma. The two-year local progression-free survival (LPFS) rate was 94.8% versus 83.2% respectively, demonstrating that PBT is not inferior to RFA treatment.[11]

Prostate Cancer

ASTRO recommends coverage of PBT for the treatment of non-metastatic prostate cancer when enrolled in an institutional review board (IRB)–approved study or a multi-institutional registry that adheres to Medicare requirements for Coverage with Evidence Development (CED).[2] NCCN guidelines note that there lacks clear evidence to support a benefit or decrement to proton therapy over IMRT for either treatment efficacy or long-term toxicity. Firm conclusions regarding differences in toxicity or effectiveness of proton and photon therapy cannot be drawn because of the limitations of the available studies.[12]

Thymomas and Thymic Carcinomas

Per NCCN, PBT has been shown to improve dosimetry compared to IMRT allowing better sparing of the normal organs (lungs, heart, and esophagus). Additionally, favorable results in terms of both local control and toxicity have been obtained with PBT. Based on these data, PBT is considered an appropriate treatment option.[13]

Hodgkin Lymphoma

Per NCCN, "Treatment with photons, electrons or protons may all be appropriate, depending on clinical circumstances. Advanced RT technologies such as intensity-modulated RT

(IMRT)/volumetric modulated arc therapy (VMAT), deep-inspiratory breath hold (DIBH) or respiratory gating, image-guided RT (IGRT), and proton therapy may offer significant and clinically relevant advantages in specific instances to spare important normal OARs and decrease the risk for late, normal tissue damage while still achieving the primary goal of local tumor control."[14(p1)]

Esophageal and Esophagogastric Junction Cancers

NCCN guidelines indicate this emerging technique may offer protection of normal tissue by limiting exposure of adjacent organs to radiation in addition to lowering the rates of post-operative pulmonary, cardiac, gastrointestinal, and wound complications. The guidelines recommend that patients with esophageal cancer be treated with PBT within a clinical trial, noting that data is early and evolving.[15] An overall low-quality body of evidence suggests that PBT has possible benefit for the treatment of esophageal adenocarcinoma (EAC). PBT may have similar effectiveness to both IMRT and 3DCRT and results in significantly reduced radiation exposure to adjacent organs at risk. PBT could possibly result in fewer complications than IMRT (intensity-modulated radiation therapy) and 3DCRT (3-dimensional conformal radiation therapy) among patients undergoing esophagectomy, however the statistical significance of these findings was mixed. The rate of nonoperative complications was comparable between PBT and IMRT.[16] According to ASTRO's 2023 Model Policy for PBT, published clinical data supports the use of PBT for primary cancers of the esophagus.[2]

Neutron Beam Therapy (NBT)

NBT utilizes neutrons, rather than photons, to destroy tumor cells. Neutrons are much heavier than photons and appear to be more effective at causing damage to very dense tumors. It is however more clinically difficult to generate neutron particles, so it has not gained wide acceptance for treatment. It has most commonly been studied in salivary gland tumors which are either unable to be removed completely or for recurrent disease.

NCCN states NBT was historically considered a promising solution for unresectable salivary gland cancer, however, they no longer recommend NBT as a general solution for salivary gland cancers due to the diminishing demand, high rates of long-term toxicity over time, concerns regarding the methodologic robustness of available randomized trial data, and closure of all but one center in the U.S. The panel recognizes the potential clinical value of neutron therapy for select patients.[3]

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2024 American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT Codes	Description
77423	High energy neutron radiation treatment delivery, 1 or more isocenter(s) with coplanar or non-coplanar geometry with blocking and/or wedge, and/or compensator(s)
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	Description
S8030	Scleral application of tantalum ring(s) for localization of lesions for proton beam therapy

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed	03/14	03/14
Annual review. References reviewed and updated. Reviewed by specialist. Changed "Last Review Date" in the header to "Date of Last Review" and "Date" in revision log to "Revision Date". Replaced ICD-10 code C78.82 with C78.2. Updated background regarding PBT for benign and low-grade central nervous system tumors in children.	11/21	11/21
Annual review completed. Removed "treated in a hypofractionated regimen" from I. D. Added "and/or neutron" to criteria III. for clarity. Background updated and minor rewording with no clinical significance. Removed ICD-10 diagnosis code table. References reviewed, reformatted and updated. External specialist reviewed.	11/22	11/22
Annual review. Updated criteria I.G. to, unresectable benign or malignant central nervous system tumors to include but not limited to primary and variant forms of astrocytoma, glioblastoma, medulloblastoma, acoustic neuroma, craniopharyngioma, benign and atypical meningiomas, pineal gland tumors, and arteriovenous malformations. Added criteria I.H., Pituitary neoplasms. Restructured and added section A. and B. to criteria II. References reviewed and updated.	11/23	11/23
Annual review. Minor rewording in Criteria I. Updated Criteria I.A. to include intraocular melanomas and removed language regarding fiducial markers. Added clarifying language to Criteria I.B. regarding primary spine or spinal cord tumors or metastatic tumors of the spine or spinal cord where organ at risk tolerance may be exceeded with photon treatments. Minor grammatical update to Criteria I.C. Updated Criteria I.D. by removing "Primary" and including intra-hepatic biliary cancers. Updated Criteria I.E. by adding "or other hematologic malignancies" and changing ≤ 18 years old to ≤ 21 years old. Updated verbiage in Criteria I.F to state "Tumors/cancers that can be treated with any other type of	11/24	11/24

Reviews, Revisions, and Approvals	Revision Date	Approval Date
radiation in members/enrollees with a known genetic mutation/syndrome." Updated verbiage in Criteria I.G. to include malignant and benign primary CNS tumors, excluding IDH wild-type glioblastoma (GBM). Added clarifying language to Criteria I.J. and removed additional language regarding when normal tissue constraints cannot be met be met by photon-based therapy. Added cancers of the nasopharynx and nasal cavity to Criteria I.J. Removed "i.e., preoperative treatment of resectable disease or primary treatment for those with unresectable disease" in Criteria I.K. Combined previous Criteria I.N. regarding thymomas and thymic carcinoma with Criteria I.M. regarding primary tumors of the mediastinum. Added Criteria I.O. for malignant pleural mesothelioma. Added Criteria I.P. for primary malignant or benign bone tumors. Added Criteria I.Q. for medically inoperable patients with a diagnosis of cancer typically treated with surgery where dose escalation is required due to the inability to receive surgery. Added Criteria I.R. for primary and metastatic tumors requiring craniospinal irradiation. Added Criteria I.S. for primary cancers of the esophagus. Added Criteria I.T. for advanced and unresectable pelvic tumors with significant pelvic and/or peri-aortic nodal disease. Added Criteria I.U. for members/enrollees 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. Added Criteria I.V. for salivary gland tumors. Minor verbiage update in Criteria II. with no impact to criteria. Background updated with no impact on criteria. References reviewed and updated. Reviewed by external specialist.		
Annual review. Added criteria under I.W. Arteriovenous Malformations (AVM). References reviewed and updated.	11/25	11/25

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.