Charged-Particle (Proton or Helium Ion) Radiotherapy

Policy # 00187
Original Effective Date: 01/26/2006
Current Effective Date: 02/15/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider charged-particle irradiation with proton or helium ion beams to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for the use of charged-particle irradiation with proton or helium ion beams may be considered when any of the following criteria are met:

- 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; or
- 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; or
- Treatment of prostate cancer,
- Treatment of pediatric central nervous system (CNS) tumors.

When Services Are Considered Investigational
Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of charged-particle irradiation with proton or helium ion beams to be investigational* when patient selection criteria are not met.

Based on review of available data, the Company considers other applications of charged-particle irradiation with proton beams to be investigational*, including but not limited to:

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

Background/Overview
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,
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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/abnormalities. However, advances in photon-based RT such as 3-D conformal RT, intensity-modulated RT (IMRT), and stereotactic body radiotherapy (SBRT) allow improved targeting of conventional therapy:

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

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

Rationale/Source

Uveal Melanomas and Skull-based Tumors
A TEC Assessment completed in 1996 on charged-particle RT for uveal melanoma and chordoma or chondrosarcoma at the skull base or cervical spine concluded that the technology is at least as effective as alternative therapies. A systematic review of charged-particle therapy found that local tumor control rate and 5-year overall survival (OS) for skull base chordomas treated with proton therapy were 63% and 81%, respectively, compared with postsurgical treatment with conventional photon therapy with reported local tumor control rates and 5-year OS of 25% and 44%, respectively, and compared with surgery followed by fractionated stereotactic radiotherapy, which resulted in a 5-year local tumor control rate of 50%. A summary of tumor control in published proton therapy studies of chondrosarcoma of the skull base was 95% five-year local tumor control, similar to the results of conventional therapy.

Charged-particle beam RT has been most extensively studied in uveal melanomas, in which the focus has been to provide adequate local control while still preserving vision. In 2013, Wang et al published a systematic review on charged-particle (proton, helium, carbon ion) RT for uveal melanoma. The review included 27 controlled and uncontrolled studies that reported health outcomes (eg, mortality, local recurrence). Three of the studies were randomized controlled trials (RCTs). One of the RCTs compared helium ion therapy with an alternative treatment (in this case, brachytherapy). The other 2 RCTs compared
different proton beam protocols so cannot be used to draw conclusions about the efficacy of charged-ion particle therapy relative to other treatments. The overall quality of the studies was low; most of the observational studies did not adjust for potential confounding variables. The analysis focused on studies of treatment-naive patients (all but one of the identified studies). In a pooled analysis of data from 9 studies, there was not a statistically significant difference in mortality with charged-particle therapy compared with brachytherapy (odds ratio [OR], 0.13; 95% confidence interval [CI], 0.01 to 1.63). However, there was a significantly lower rate of local control with charged-particle therapy compared with brachytherapy in a pooled analysis of 14 studies (OR=0.22; 95% CI, 0.21 to 0.23). There were significantly lower rates of radiation retinopathy and cataract formation in patients treated with charged-particle therapy compared with brachytherapy (pooled rates of 0.28 vs 0.42 and 0.23 vs 0.68, respectively). According to this review, there is low-quality evidence that charged-particle therapy is at least as effective as alternative therapies as primary treatment of uveal melanoma and is better at preserving vision.

Another RCT, published in 2015 by Mishra et al, compared charged-particle therapy using helium ions and iodine 125 (I-125) plaque therapy in 184 patients with uveal melanoma. The primary end point was local tumor control. Median follow-up was 14.6 years in the charged-particle therapy group and 12.3 years in the I-125 plaque therapy group. The rate of local control at 12 years was significantly higher in the helium ion group (98%; 95% CI, 88% to 100%) than in the I-125 plaque therapy group (79%; 95% CI, 68% to 87%; p=0.006). OS at 12 years was 67% (95% CI, 55% to 76%) in the helium ion group and 54% (95% CI, 43% to 63%) in the I-125 plaque therapy group (p=0.02).

Skull-Based Tumors
A 2016 systematic review by Matloob et al evaluated the literature on proton beam therapy for skull-based chordomas. The review included controlled trials and case series with more than 5 patients. Twelve studies met eligibility criteria. The authors did not report study type, but they did not appear to identify only controlled trials, only case series. Sample sizes ranged from 9 to 367 patients. Six studies reported a 5-year survival rates that ranged from 67% to 94%.

Pediatric Central Nervous System Tumors
Radiation therapy is an integral component of the treatment of many pediatric CNS tumors including high-grade gliomas, primitive neuroectodermal tumors (PNETs), medulloblastomas, ependymomas, germ cell tumors, some craniopharyngiomas and subtotally resected low-grade astrocytomas. Children who are cured of their tumor experience long-term sequelae of radiation treatment, which may include developmental, neurocognitive, neuroendocrine, and hearing late effects. Radiation to the cochlea may lead to loss of hearing at doses greater than 35-45 Gy in the absence of chemotherapy, and the risk of ototoxicity is increased in children who receive ototoxic platinum-based chemotherapy regimens. Craniospinal irradiation, most commonly used in the treatment of medulloblastoma, has been reported to lead to thyroid dysfunction and damage to the lungs, heart and gastrointestinal tract. In addition, patients who receive radiation at a young age are at an increased risk of developing radiation-induced second tumors compared to their adult counterparts. The development of more conformal radiation techniques has decreased inadvertent radiation to normal tissues; however, while IMRT decreases high doses to nearby normal tissues, it delivers a larger volume of low- and intermediate-dose radiation. Proton beam therapy eliminates the exit dose to normal tissues and may eliminate about 50% of radiation to normal tissue.
Merchant and colleagues sought to determine whether proton radiotherapy has clinical advantages over photon radiotherapy in childhood brain tumors. Three-dimensional imaging and treatment-planning data, which included targeted tumor and normal tissues contours, were acquired for 40 patients. Histologic subtypes in the 40 patients were 10 each with optic pathway glioma, craniopharyngioma, infratentorial ependymoma, or medulloblastoma. Dose-volume data were collected for the entire brain, temporal lobes, cochlea, and hypothalamus, and the data were averaged and compared based on treatment modality (protons vs. photons) using dose-cognitive effects models. Clinical outcomes were estimated over 5 years. With protons (compared to photons), relatively small critical normal tissue volumes (e.g. cochlea and hypothalamus) were spared from radiation exposure when not adjacent to the primary tumor volume. Larger normal tissue volumes (e.g. supratentorial brain or temporal lobes) received less of the intermediate and low doses. When these results were applied to longitudinal models of radiation dose-cognitive effects, the differences resulted in clinically significant higher intelligence quotient (IQ) scores for patients with medulloblastoma and craniopharyngioma and academic reading scores in patients with optic pathway glioma. There were extreme differences between proton and photon dose distributions for the patients with ependymoma, which precluded meaningful comparison of the effects of protons versus photons. The authors concluded that the differences in the overall dose distributions, as evidenced by modeling changes in cognitive function, showed that these reductions in the lower-dose volumes or mean dose would result in long-term, improved clinical outcomes for children with medulloblastoma, craniopharyngioma, and glioma of the optic pathway.

In 2016, Leroy et al published a systematic review of the literature on PBT for treatment of pediatric cancers. Their findings on pediatric CNS tumors include the following:

- **Craniopharyngioma:** Three studies were identified, 2 retrospective case series and 1 retrospective comparative study of PBT versus IMRT. They concluded that there is very low level evidence that survival outcomes are similar with PBT and IMRT.
- **Ependymoma:** One prospective case series and 1 retrospective case series were identified. They concluded that the evidence is insufficient to support or refute the use of PBT for this condition.
- **Medulloblastoma:** One prospective case series and 2 retrospective case series were identified. They concluded that the evidence is insufficient to support or refute the use of PBT for this condition.
- **CNS germinoma:** One retrospective case series was identified. They concluded that the evidence is insufficient to support or refute the use of PBT for this condition.

Representative series of PBT in multiple pediatric CNS tumor types are described next.

Loma Linda University Medical Center reported on proton radiation in the treatment of low-grade gliomas in 27 pediatric patients. Six patients experienced local failure; acute side effects were minimal. After a median follow-up of 3 years, all of the children with local control maintained performance status. A dosimetric comparison of protons to photons for 7 optic pathway gliomas treated at Loma Linda showed a decrease in radiation dose to the contralateral optic nerve, temporal lobes, pituitary gland and optic chiasm with the use of protons.
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MD Anderson Cancer Center and Methodist Hospital in Houston reported on 52 children treated at 2 centers in Texas; 21 received PBT and 31 received IMRT. Patients received a median dose of 50.4 Gy. At 3 years, OS was 94.1% in the PBT group and 96.8% in the IMRT group (p=0.742). Three-year nodular and cystic failure-free survival rates were also similar between groups. Seventeen patients (33%) were found on imaging to have cyst growth within 3 months of RT, and 14 patients had late cyst growth (>3 months after therapy); rates did not differ significantly between groups. In 14 of the 17 patients with early cyst growth, enlargement was transient.

Massachusetts General Hospital reported on the use of protons to treat germ cell tumors in 22 patients, 13 with germinoma and 9 with nongerminomatous germ cell tumors (NGGCTs). Radiation doses ranged from 30.6 to 57.6 cobalt Gray equivalents (CGE). All NGGCT patients received chemotherapy before RT. Twenty-one patients were treated with cranial spinal irradiation, whole ventricular RT, or whole-brain radiation followed by an involved field boost; 1 patient received involved field alone. Median follow-up was 28 months. There were no CNS recurrences or deaths. Following RT, 2 patients developed growth hormone deficiency and 2 patients developed central hypothyroidism. The authors stated that longer follow-up was necessary to assess the neurocognitive effects of therapy. In the same study, a dosimetric comparison of photons and protons for representative treatments with whole ventricular and involved field boost was done. Proton RT provided substantial sparing to the whole brain and temporal lobes, and reduced doses to the optic nerves.

Moeller and colleagues reported on 23 children who were enrolled in a prospective observational study and treated with PBT for medulloblastoma between the years 2006-2009. As hearing loss is common following chemoradiotherapy for children with medulloblastoma, the authors sought to compare whether proton radiotherapy led to a clinical benefit in audiometric outcomes (since, compared to photons, protons reduce radiation dose to the cochlea for these patients). The children underwent pre- and 1-year post-radiotherapy pure-tone audiometric testing. Ears with moderate-to-severe hearing loss prior to therapy were censored, leaving 35 ears in 19 patients available for analysis. The predicted mean cochlear radiation dose was 30 60Co-Gy Equivalents (range 19-43). Hearing sensitivity significantly declined following radiotherapy across all frequencies analyzed (p < 0.05). There was partial sparing of mean post-radiation hearing thresholds at low-to-midrange frequencies; the rate of high-grade (grade 3 or 4) ototoxicity at 1 year was 5%. The authors compared this to a rate of grade 3-4 toxicity following IMRT of 18% in a separate case series. The authors concluded that preservation of hearing in the audible speech range, as observed in their study, may improve both quality of life and cognitive functioning for these patients.

Pediatric Non-Central Nervous System Tumors
There is scant data on the use of PBT in pediatric non-CNS tumors and includes dosimetric planning studies in a small number of pediatric patients with parameningeal rhabdomyosarcoma and late toxicity outcomes in other solid tumors of childhood.

Non-Small Cell Lung Cancer
A 2010 TEC Assessment assessed the use of PBT for NSCLC. This TEC Assessment addressed the key question of how health outcomes (OS, disease-specific survival, local control, disease-free survival, and adverse events) with PBT compare with outcomes observed for SBRT, which is an accepted approach for
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using RT to treat NSCLC. Eight PBT case series were identified in the Assessment that included a total of 340 patients. No comparative studies, randomized or nonrandomized, were found. For these studies, stage I comprised 88.5% of all patients, and only 39 patients were in other stages or had recurrent disease. Among 7 studies reporting 2-year OS, probabilities ranged between 39% and 98%. At 5 years, the range across 5 studies was 25% to 78%.

The report concluded that the evidence is insufficient to permit conclusions about the results of PBT for any stage of NSCLC. All PBT studies are case series; there are no studies directly comparing PBT and SBRT. Among study quality concerns, no study mentioned using an independent assessor of patient-reported adverse events; adverse events were generally poorly reported, and details were lacking on several aspects of PBT treatment regimens. The PBT studies were similar in patient age, but there was great variability in percent within stage IA, sex ratio, and percent medically inoperable. There is a high degree of treatment heterogeneity among the PBT studies, particularly with respect to planning volume, total dose, number of fractions, and number of beams. Survival results are highly variable. It is unclear whether the heterogeneity of results can be explained by differences in patient and treatment characteristics. In addition, indirect comparisons between PBT and SBRT, comparing separate sets of single-arm studies on PBT and SBRT may be distorted by confounding. Absent RCTs, the comparative effectiveness of PBT and SBRT was found to be uncertain. The Assessment noted that adverse events reported after PBT generally fell into several categories: rib fracture, cardiac, esophageal, pulmonary, skin, and soft tissue. Adverse events data in PBT studies are difficult to interpret due to lack of consistent reporting across studies, lack of detail about observation periods, and lack of information about rating criteria and grades.

A 2010 indirect meta-analysis reviewed in the TEC Assessment found a nonsignificant difference of 9 percentage points between pooled 2-year OS estimates favoring SBRT over PBT for treatment of NSCLC. The nonsignificant difference of 2.4 percentage points at 5 years also favored SBRT over PBT. Based on separate groups of single-arm studies on SBRT and PBT, it is unclear if this indirect meta-analysis adequately addressed the possible influence of confounding on the comparison of SBRT and PBT.

Pijls-Johannesma et al conducted a 2010 systematic literature review through November 2009 examining the evidence on the use of particle therapy in lung cancer. Study inclusion criteria included that the series had at least 20 patients and a follow-up period of 24 months or more. Eleven studies, all dealing with NSCLC, mainly stage I, were included in the review, 5 investigating protons (n=214) and 6, C-ions (n=210). The proton studies included 1 phase 2 study, 2 prospective studies, and 2 retrospective studies. The C-ion studies were all prospective and conducted at the same institution in Japan. No phase 3 studies were identified. Most patients had stage 1 disease, however, a wide variety of radiation schedules were used, making comparisons of results difficult and local control rates were defined differently across studies. For proton therapy, 2- to 5-year local tumor control rates varied in the range of 57% to 87%. The 2- and 5-year OS and 2- and 5-year cause-specific survival (CSS) rates were 31% to 74% and 23% and 58% to 86% and 46%, respectively. These local control and survival rates are equivalent to or inferior to those achieved with stereotactic radiotherapy. Radiation-induced pneumonitis was observed in about 10% of patients. For C-ion therapy, the overall local tumor control rate was 77%, but it was 95% when using a hypofractionated radiation schedule. The 5-year OS and CSS rates were 42% and 60%, respectively. Slightly better results were reported when using hypofractionation, 50% and 76%, respectively. The authors concluded that
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although the results with protons and heavier charged particles were promising, additional well-designed trials are needed.

To date, no RCTs or nonrandomized trials comparing health outcomes in patients treated with PBT to an alternative treatment have been published.

Head and Neck Tumors, Other than Skull-based
A 2014 systematic review evaluated the literature on charged-particle therapy versus photon therapy for the treatment of paranasal sinus and nasal cavity malignant disease. The authors identified 41 observational studies that included 13 cohorts treated with charged-particle therapy (total N=286 patients) and 30 cohorts treated with photon therapy (total N=1186 patients). There were no head-to-head trials. In a meta-analysis, the pooled event rate of OS was significantly higher with charged-particle therapy than photon therapy at the longest duration of follow-up (risk ratio [RR], 1.27; 95% CI, 1.01 to 1.59). Findings were similar for the outcome survival at 5 years (RR=1.51; 95% CI, 1.14 to 1.99). Findings were mixed for the outcomes locoregional control and disease-free survival; photon therapy was significantly better for only 1 of the 2 timeframes (longest follow-up or 5-year follow-up). In terms of adverse effects, there were significantly more neurologic toxic effects with charged-particle therapy compared with photon therapy (p<0.001) but other toxic adverse event rates (eg, eye, nasal, hematologic) did not differ significantly between groups. The authors noted that the charged-particle studies were heterogeneous (eg, type of charged particles [carbon ion, proton]), and delivery techniques. It should also be noted that comparisons were indirect, and none of the studies included in the review actually compared the 2 types of treatment in the same patient sample.

Also in 2015, Zenda et al reported on late toxicity in 90 patients after PBT for nasal cavity, paranasal sinuses, or skull base malignancies. Eighty seven of the 90 patients had paranasal sinus or nasal cavity cancer. The median observation period was 57.5 months. Grade 3 late toxicities occurred in 17 patients (19%) and grade 4 occurred in 6 patients (7%). Five patients developed cataracts, and 5 had optic nerve disorders. Late toxicities (other than cataracts) developed a median of 39.2 months after PBT.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

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

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

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

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

For individuals who have head and neck tumors other than skull-based who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes. The
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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.

Clinical Input Received through Physician Specialty Society and Academic Medical Center

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 2 physician specialty societies (4 responses) and 4 academic medical centers. There was uniform support for the use of PBT in pediatric CNS tumors. Two reviewers expressed support for the use of PBT in pediatric non-CNS tumors; data for this use are scant. Input on head and neck tumors (non-skull based) was mixed.

References
2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Charged particle (proton or helium ion) irradiation for uveal melanoma and for chordoma or chondrosarcoma of the skull base or cervical spine. TEC Assessments 1996; Volume 11, Tab 1.
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10/05/2005 Medical Director review
12/20/2005 Medical Policy Committee review
01/26/2006 Quality Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
09/20/2006 Medical Policy Committee approval. Coverage eligibility changed for the treatment of prostate cancer from not medically necessary to "eligible for coverage".
12/06/2006 Medical Director review
02/13/2008 Medical Director review
02/20/2008 Medical Policy Committee approval
02/04/2009 Medical Director review
02/19/2009 Medical Policy Committee approval. No change to coverage eligibility.
02/04/2010 Medical Policy Committee review
02/17/2010 Medical Policy Implementation Committee approval. No change to coverage eligibility. Rationale replaced.
02/03/2011 Medical Policy Committee review
02/16/2011 Medical Policy Implementation Committee approval. New investigational statement added.
02/02/2012 Medical Policy Committee review
02/15/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/07/2013 Medical Policy Committee review
02/20/2013 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2014 Medical Policy Committee review

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02/19/2014 Medical Policy Implementation Committee approval. Added that proton radiotherapy may be considered eligible for coverage with criteria for the treatment of pediatric central nervous system tumors. Investigational statements added for pediatric non-central nervous system tumors and head and neck tumors (non-skull based).

02/05/2015 Medical Policy Committee review
02/18/2015 Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
02/04/2016 Medical Policy Committee review
02/17/2016 Medical Policy Implementation Committee approval. Title change
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
02/02/2017 Medical Policy Committee review
02/15/2017 Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 02/20/2018

**Coding**

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2016 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
   A. In accordance with nationally accepted standards of medical practice;
   B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
   C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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