



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Stem-Cell Transplantation for Central Nervous System Tumors

Effective Date 7/15/2011
Next Review Date.....7/15/2012
Coverage Policy Number 0369

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	4
References	6
Policy History.....	10

Hyperlink to Related Coverage Policies

Stem-Cell Transplantation for Neuroblastoma
Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT)

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers autologous hematopoietic stem-cell transplantation (HSCT) following high-dose chemotherapy as medically necessary for the treatment of EITHER of the following central nervous system tumors:

- primitive neuroectodermal tumor (PNET)
- previously untreated or recurrent medulloblastoma

For information on coverage of stem-cell transplantation for neuroblastoma, refer to the CIGNA Coverage Policy Stem-Cell Transplantation for Neuroblastoma.

CIGNA does not cover autologous hematopoietic stem-cell transplantation (HSCT) for the treatment of ANY of the following central nervous system tumors because it is considered experimental, investigational or unproven (this list may not be all inclusive):

- astrocytoma
- brainstem glioma
- ependymoma
- oligodendroglioma

CIGNA does not cover allogeneic hematopoietic stem-cell transplantation (HSCT) for the treatment of central nervous system tumors.

General Background

Primary central nervous system (CNS) tumors are a diverse group of tumors originating in the brain or spinal cord. CNS tumors, develop from different cell types, form in different areas of the CNS and may have different prognoses and treatment in children compared with adults (American Cancer Society [ACS], 2010b). Tumor types include, but are not limited to medulloblastoma/primitive neuroectodermal tumors, astrocytoma, glioma, and ependymoma.

In both children and adults, tumor location and extent of spread play important roles in treatment and prognosis. Despite the use of multimodality treatment involving surgery, radiotherapy and chemotherapy, the cure rate remains low in high-risk histological types, and for individuals with residual, recurrent or disseminated disease. Systemic chemotherapy is generally less effective because of the blood-brain barrier, which prevents many chemotherapeutic agents from reaching the brain (National Cancer Institute [NCI], 2010[a, b]).

CNS tumors are more common in children than adults and constitute the most common solid tumors of childhood. For most primary brain tumors in children, the optimal treatment regimens have not been determined. Overall, these central nervous system (CNS) tumors have a relatively poor prognosis.

In an attempt to eradicate residual neoplastic cells and improve cure rate high-dose chemotherapy with autologous hematopoietic stem-cell transplantation (HSCT) has been investigated as a treatment option for selected individuals with certain high-risk CNS tumors.

Stem-Cell Transplantation

HSCT refers to transplantation of hematopoietic stem cells from a donor into a patient. HSCT can be either autologous (i.e., using the patient's own stem cells) or allogeneic (i.e., using stem cells from a donor).

Autologous HSCT: High-dose chemotherapy and autologous HSCT has been used as frontline, as well as salvage therapy with a variety of CNS malignancies. Results vary based on the ability of each strategy to allow better penetration of the blood brain barrier and to increase the dose-response effect. Myeloablative therapy may initially delay, and later avoid the use of radiotherapy in infants and toddlers (Kadota, 2008).

The use of tandem autologous transplantation for the treatment of central nervous system (CNS) tumors is the subject of ongoing research. At this time it is still unknown whether the use of this therapy for patients with bulky residual tumor or for heavily pretreated patients will improve outcome compared with single-cycle myeloablative chemotherapy regimens (Marachelian, 2008). Gill et al. (2008) performed a retrospective review comparing the results of adult patients (i.e. ≥ 18 years) with recurrent central nervous system tumors who received HSCT (n=10) or conventional-dose therapy (n=13). Of the patients undergoing transplantation (n=10) eight had a diagnosis of medulloblastoma; two patients were diagnosed with neuroblastoma. Six patients received tandem autologous HSCT; four patients received a single autologous HSCT. Transplantation was associated with increased survival (p=.044) compared with those receiving conventional chemotherapy. There was an improvement in time-to-progression for patients who received tandem versus a single dose of myeloablative chemotherapy (p=0.46); however, no improvement in survival was seen (p=0.132).

Allogeneic HSCT: There are scarce data regarding the safety and effectiveness of allogeneic HSCT for the treatment of CNS tumors. The role of allogeneic HSCT has not yet been established for this indication.

Medulloblastoma/Primitive Neuroectodermal Tumor: Medulloblastoma and supratentorial primitive neuroectodermal tumor (sPNET) may be responsive to conventional chemotherapy; however, while 30–50% of patients will have objective response, long-term disease control with conventional therapy is rare. In adults over age 45, 90% of brain tumors are gliomas, with over 77% of these being high-grade.

Treatment options for individuals with medulloblastoma or primitive neuroectodermal tumors may include combination chemotherapy, systemic and oral chemotherapy plus intrathecal chemotherapy; higher-dose chemotherapy supported by autologous bone marrow rescue or peripheral stem cell rescue, and chemotherapy followed by radiation therapy to the primary tumor site. High-dose chemotherapy is also under clinical evaluation

for patients with newly diagnosed pineoblastoma, and pineal parenchymal tumors of intermediate differentiation (NCI, 2011[c]).

Literature Review

There are limited data from randomized controlled trials regarding the safety and effectiveness of hematopoietic stem-cell transplantation (HSCT) for medulloblastoma or primitive neuroectodermal tumors (PNET). Outcomes from several prospective trials, case series, and retrospective studies demonstrate improved response rates, and disease-free-, event-free- and/or overall survival with the use of high-dose chemotherapy and autologous HSCT for primary brain tumors, including medulloblastoma and PNET. Five-year overall survival (OS) rates range from 85–39%; event-free survival (EFS) ranged from 83%–49% (Dunkel, 2010; Chintagumpala, 2009; Grodman, 2009; Cheuk, 2008; Fangusaro, 2008a; Ridola, 2008; Sung, 2007; Gajjar, 2006; Chi, 2004).

Although data are not robust, improved response rates, and improved EFS and OS have been demonstrated in a number of uncontrolled prospective and retrospective studies.

Astrocytoma: High-grade astrocytic tumors are often locally invasive and extensive (National Cancer Institute [NCI], 2011[d]). According to the NCI, patients for whom initial treatment fails may benefit from additional treatment, including high-dose, marrow-ablative chemotherapy with HSCT.

Literature Review

Finlay et al. (2008) reported the results of 27 children and adolescents with malignant astrocytomas, glioblastoma multiforme, or anaplastic astrocytoma who received myeloablative chemotherapy followed by autologous hematopoietic stem-cell transplantation (HSCT) with one of three chemotherapy regimens following initial tumor progression. Event-free survival (EFS) and mortality rates following myeloablative chemotherapy for these patients was compared with outcomes of a cohort of similar patients who received only conventional chemotherapy following initial tumor progression. No significant differences in overall survival (OS) were noted between the two groups when not stratified according to whether patients were surgically debulked prior to treatment ($p=0.39$). When patients were stratified according to surgical debulking, differences in survival were statistically significant ($p=.017$).

Although results are promising, the ability to draw conclusions regarding improved health outcomes with this treatment is limited by study design and small patient population. The role of HSCT for this indication has not yet been established.

Brainstem Glioma: In brainstem gliomas, the use of more aggressive chemotherapy strategies including high-dose chemotherapy followed by PBSC reinfusion results in relatively brief-duration responses and few instances of significant tumor reduction lasting 12 months or longer (Maity, 2008).

Literature Review

Bay et al. (2007) reported the results of a retrospective study sponsored by the European Group for Blood and Marrow Transplantation. Two-hundred seventeen patients with high-grade supratentorial glioma underwent high-dose chemotherapy followed by autologous HSCT. The median age was 44.8 years. Treatment-related mortality was 4.5%. With a median follow-up of eight years, the median OS was 20 months. The survival probabilities at 6 months, 1, 5 and 10 years were 84%, 62%, 32%, and 17%, respectively. At the time of the study publication, the authors reported that only five patients (8%) were alive.

Data are lacking in the published peer-reviewed scientific literature regarding the safety and effectiveness of HSCT for the treatment of glioma. The role of HSCT has not yet been established for this indication.

Ependymoma: There are scarce data in the published peer-reviewed scientific literature regarding the safety and effectiveness of HSCT for this indication. The role of this therapy has not yet been established for this indication.

Oligodendroglioma: There are scarce data in the published peer-reviewed scientific literature regarding the safety and effectiveness of HSCT for the treatment of oligodendroglioma. The role of this therapy has not yet been established for this indication.

Contraindications

Many factors affect the outcome of tissue transplantation; the selection process is designed to obtain the best result for each individual. The presence of any significant comorbid conditions which would significantly compromise clinical care and chances of survival is a contraindication to transplant. Relative contraindications to hematopoietic stem-cell transplantation (HSCT) include, but are not limited to:

- poor cardiac function (ejection fraction less than 45%)
- poor liver function (bilirubin greater than 2.0 mg/dL and transaminases greater than two times normal)
- poor renal function (creatinine clearance less than 50 mL/min)
- poor pulmonary function (diffusion capacity [DLCO] less than 60% of predicted)
- presence of human immunodeficiency virus or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus
- Karnofsky rating less than 60% and/or Eastern Cooperative Oncology Group (ECOG) performance status greater than two

Professional Societies/Organizations

National Cancer Institute (NCI): The NCI lists various therapies, including high-dose chemotherapy with autologous stem-cell rescue, as standard treatment options for central nervous system tumors in children:

- **Medulloblastoma:** According to the NCI (2010 [c]), standard treatment options for children ≤ 3 years with newly-diagnosed medulloblastoma continue to evolve and may include utilizing higher-dose chemotherapeutic regimens supported by autologous stem cell rescue or peripheral stem cell rescue. "Results of trials utilizing higher-dose, marrow ablative, chemotherapeutic regimens supported by autologous stem cell rescue or peripheral stem cell rescue have also demonstrated that a subgroup of patients with medulloblastoma who are younger than 3 years at the time of diagnosis can be treated with chemotherapy alone." The NCI also notes that for children >3 years with poor-risk medulloblastoma or pineoblastoma a variety of different treatment approaches are under evaluation, including the use of higher doses of chemotherapy supported by supported by autologous bone marrow rescue or peripheral stem cell rescue.
- **Primitive Neuroectodermal Tumor (PNET):** For children with newly diagnosed supratentorial primitive neuroectodermal tumors <3 years, the NCI (2011[c]) notes that treatment is similar to that outlined for the treatment of medulloblastoma. The chemotherapeutic approaches for children >3 years are also similar to those used for children with poor-risk medulloblastoma.
- **Diffuse Intrinsic Pontine Glioma:** The NCI (2011[a]) notes that high-dose, marrow-ablative chemotherapy with autologous hematopoietic stem cell rescue has been ineffective in extending survival.
- **High-Grade Childhood Recurrent Cerebral Astrocytoma:** The NCI (2011[d]) notes that high-dose chemotherapy with hematopoietic stem cell transplant may be effective in a subset of children with minimal residual disease at time of treatment. These children should also be considered for entry into trials of novel therapeutic approaches.

National Comprehensive Cancer Network Guidelines™ (NCCN Guidelines™): Regarding medulloblastoma and supratentorial PNET, the NCCN (2011) notes "High-dose chemotherapy in combination with autologous stem-cell transplantation is a feasible strategy for patients who have had a good response to lower doses."

Summary

Although the data are not robust, the published peer-reviewed scientific literature supports the safety and effectiveness of autologous hematopoietic stem-cell transplantation (HSCT) following high-dose chemotherapy for the treatment of previously untreated or recurrent medulloblastoma and primitive neuroectodermal tumor (PNET). Data are lacking to support the safety and effectiveness of autologous HSCT for other CNS tumors, including but not limited to, astrocytoma, brainstem glioma, ependymoma, and oligodendroglioma. There are insufficient data to support the safety and effectiveness of allogeneic HSCT for CNS tumors.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary when used to report autologous bone marrow or blood-derived stem cell procedures for medulloblastoma/primitive neuroectodermal tumors (PNET):

CPT[®]* Codes	Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell remover
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear or buffy coat layer
38230	Bone marrow harvesting for transplantation
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous

HCPCS Codes	Description
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

ICD-9-CM Diagnosis Codes	Description
191.0-191.9	Malignant neoplasm of brain
192.0-192.9	Malignant neoplasm of other and unspecified parts of nervous system
237.5	Neoplasm of uncertain behavior of brain and spinal cord

Experimental/Investigational/Unproven/Not Covered when used to report autologous bone marrow or blood-derived stem cell procedures for any other CNS tumors including astrocytoma, brainstem glioma, ependymoma, and oligodendroglioma:

CPT[®]* Codes	Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion

38212	Transplant preparation of hematopoietic progenitor cells; red blood cell remover
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear or buffy coat layer
38230	Bone marrow harvesting for transplantation
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous

HCPCS Codes	Description
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

ICD-9-CM Diagnosis Codes	Description
191.0-191.9	Malignant neoplasm of brain
192.0-192.9	Malignant neoplasm of other and unspecified parts of nervous system
237.5	Neoplasm of uncertain behavior of brain and spinal cord

Experimental/Investigational/Unproven/Not Covered when used to report allogeneic bone marrow or blood-derived stem cell procedures:

CPT* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38240	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions

HCPCS Codes	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem cell transplantation, allogeneic

ICD-9-CM Diagnosis Codes	Description
191.0-191.9	Malignant neoplasm of brain
192.0-192.9	Malignant neoplasm of other and unspecified parts of nervous system
237.5	Neoplasm of uncertain behavior of brain and spinal cord

***Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.**

References

1. Abrey LE, Childs BH, Paleologos N, Kaminer L, Rosenfeld S, Salzman D, et al. High-dose chemotherapy with stem cell rescue as initial therapy for anaplastic oligodendroglioma. J Neuro Oncol. 2003 Nov;65(2):127-34. (a)

2. Abrey LE, Childs BH, Paleologos N, Kaminer L, Rosenfield S, Salzman D, et al. High-dose chemotherapy with stem cell rescue as initial therapy for anaplastic oligodendroglioma: long-term follow-up. *Neuro Oncol.* 2006 Apr;8(2):183-8. Epub 2006 Mar 8.(b)
3. American Cancer Society. (a) Brain and spinal cord tumors in adults. Updated 2011 May 9. Accessed May 24, 2011. Available at URL address: <http://documents.cancer.org/103.00/103.00.pdf>
4. American Cancer Society. (b) Brain and spinal cord tumors in children. Updated 2010 Nov 12. Accessed May 24, 2011. Available at URL address: <http://documents.cancer.org/144.00/144.00.pdf>
5. Bay JO, Claude L, Pierre B, Xavier D, Pierre V, Fabrice K, et al. Does high-dose carmustine increase overall survival in supratentorial high-grade malignant glioma? An EBMT retrospective study. *Int J Cancer.* 2007 Apr 15;120(8):1782-6.
6. Chen B, Ahmed T, Mannancheril A, Gruber M, Benzil DL. Safety and efficacy of high-dose chemotherapy with autologous stem cell transplantation for patients with malignant astrocytomas. *Cancer.* 2004;100:2201-7.
7. Cheuk DK, Lee TL, Chiang AK, Ha SY, Chan GC. Autologous hematopoietic stem cell transplantation for high-risk brain tumors in children. *J Neuro Oncol.* 2008 Feb;86(3):337-47. Epub 2007 Sep 29.
8. Chi SN, Gardner SL, Levy AS, Knopp EA, Miller DC, Wisoff JH, et al. Feasibility and response to induction chemotherapy intensified with high-dose methotrexate for young children with newly diagnosed high-risk disseminated medulloblastoma. *J Clin Oncol.* 2004 Dec 15;22(24):4881-7.
9. Chintagumpala M, Hassall T, Palmer S, Ashley D, Wallace D, Kasow K, et al. A pilot study of risk-adapted radiotherapy and chemotherapy in patients with supratentorial PNET. *Neuro Oncol.* 2009 Feb;11(1):33-40.
10. Colombat P, Lemeval A, Bertrand P, Dewail V, Rachieru P, Brion A, et al. High-dose chemotherapy with autologous stem cell transplantation as first-line therapy for primary CNS lymphoma in patients younger than 60 years: a multicenter phase II study of the GOELAMS group. *Bone Marrow Transplant.* 2006 Sep;38(6):417-20.
11. Dunkel IJ, Gardner SL, Garvin JH Jr, Goldman S, Shi W, Finlay JL. High dose carboplatin, thiotepa and etoposide with autologous stem-cell rescue for patients with previously irradiated recurrent medulloblastoma. *Neuro Oncol.* 2010 Mar;12(3):297-303.
12. Durando X, Lemaire JJ, Tortochaux J, Van-Praagh I, Kwiatkowski F, Vincent C, et al. High-dose BCNU followed by autologous hematopoietic stem cell transplantation in supratentorial high-grade malignant gliomas: a retrospective analysis of 114 patients. *Bone Marrow Transplant.* 2003 Apr;31(7):559-64.
13. ECRI Institute. Hotline Response [database online]. Plymouth Meeting (PA): ECRI Institute, 2008 Jul 16. High-Dose Chemotherapy with Stem Cell Transplantation for Primary Brain Tumors. 2008 Jul 16. Available at URL address: [http:// www.ecri.org](http://www.ecri.org).
14. Fangusaro JR, Finlay J, Sposto R, Ji L, Saly M, Zacharoulis S, et al. Intensive chemotherapy followed by consolidative myeloablative chemotherapy with autologous hematopoietic cell rescue (AuHCR) in young children with newly diagnosed supratentorial primitive neuroectodermal tumors (sPNETs): report of the Head Start I and II experience. *Pediatr Blood Cancer.* 2008 Feb;50(2):312-8. (a)
15. Fangusaro JR, Jubran RF, Allen J, Gardner S, Dunkel IJ, Rosenblum M, et al. Brainstem primitive neuroectodermal tumors (bstPNET): results of treatment with intensive induction chemotherapy followed by consolidative chemotherapy with autologous hematopoietic cell rescue. *Pediatr Blood Cancer.* 2008 Mar;50(3):715-7. (b)
16. Finlay JL, Dhall G, Boyett JM, Dunkel IJ, Gardner SL, Goldman S, et al. Myeloablative chemotherapy with autologous bone marrow rescue in children and adolescents with recurrent malignant astrocytoma:

outcome compared with conventional chemotherapy: a report from the Children's Oncology Group. *Pediatr Blood Cancer*. 2008 Dec;51(6):806-11.

17. Gajjar A. High-dose chemotherapy for recurrent medulloblastoma: time for a reappraisal. *Cancer*. 2008 Apr 15;112(8):1643-5.
18. Gajjar A, Chintagumpala M, Ashley D, Kellie S, Kun LE, Merchant TE, et al. Risk-adapted craniospinal radiotherapy followed by high-dose chemotherapy and stem-cell rescue in children with newly diagnosed medulloblastoma (St Jude Medulloblastoma-96): long-term results from a prospective, multicentre trial. *Lancet Oncol*. 2006 Oct;7(10):813-20. Erratum in: *Lancet Oncol*. 2006 Oct;7(10):797
19. Gill P, Litzow M, Buckner J, Arndt C, Moynihan T, Christianson T, et al. High-dose chemotherapy with autologous stem cell transplantation in adults with recurrent embryonal tumors of the central nervous system. *Cancer*. 2008 Apr 15;112(8):1805-11.
20. Grill J, DeFour C, Kalifa C. High-dose chemotherapy in children with newly-diagnosed medulloblastoma. *Lancet Oncol*. 2006 Oct;7(10):787-9.
21. Grill J, Le Deley MC, Gambarelli D, Raquin MA, Couanet D, Pierre-Kahn A, et al. Postoperative chemotherapy without irradiation for ependymoma in children under 5 years of age: a multicenter trial of the French Society of Pediatric Oncology. *J Clin Oncol*. 2001 Mar 1;19(5):1288-96.
22. Grodman H, Wolfe L, Kretschmar C. Outcome of patients with recurrent medulloblastoma or central nervous system germinoma treated with low dose continuous intravenous etoposide along with dose-intensive chemotherapy followed by autologous hematopoietic stem cell rescue. *Pediatr Blood Cancer*. 2009 Jul;53(1): 33-6.
23. Gururangan S, McLaughlin C, Quinn J, Rich J, Reardon D, Halperin EC, et al. High-dose chemotherapy with autologous stem-cell rescue in children and adults with newly diagnosed pineoblastomas. *J Clin Oncol*. 2003 Jun 1;21(11):2187-91.
24. Kadota RP, Mahoney DH, Doyle J, Duerst R, Friedman H, Holmes E, et al. Dose intensive melphalan and cyclophosphamide with autologous hematopoietic stem cells for recurrent medulloblastoma or germinoma. *Pediatr Blood Cancer*. 2008 Nov;51(5):675-8.
25. Kuttesch JF, Ater JL. Brain tumors in childhood. In: Kleigman RM, Behrman RE, Jenson HB, Stanton BF, editors. *Nelson textbook of pediatrics*. 18th ed. Philadelphia (PA): Saunders Elsevier;2007.
26. MacDonald TJ, Arenson EB, Ater J, Sposto R, Bevan HE, Brunner J, et al. Phase II study of high-dose chemotherapy before radiation in children with newly diagnosed high grade astrocytoma: final analysis of children's cancer group study 9933. *Cancer*. 2005 Dec 15(104)12: 2862-71.
27. Maity A, Pruitt AA, Judy KD, Phillips PC, Lustig R. Cancer of the central nervous system. In: Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, editors. *Abeloff's Clinical Oncology*. 4th ed. New York: Churchill Livingstone;2008.
28. Marachelian A, Butturini A, Finlay J. Myeloablative chemotherapy with autologous hematopoietic progenitor cell rescue for childhood central nervous system tumors. *Bone Marrow Transplant*. 2008 Jan;41(2):167-72.
29. Massimino M, Gandola L, Spreafico F, Luksch R, Collini P, Giangaspero F, et al. Supratentorial primitive neuroectodermal tumors (S-PNET) in children: A prospective experience with adjuvant intensive chemotherapy and hyperfractionated accelerated radiotherapy. *Int J Radiat Oncol Biol Phys*. 2006 Mar 15;64(4):1031-7. Epub 2005 Dec 15.
30. Montemurro M, Kiefer T, Schuler F, Ali-Ali HK, Wolf HH, Herbst R, et al. Primary central nervous system lymphoma treated with high-dose methotrexate, high-dose busulfan/thiotepa, autologous stem-cell transplantation and response-adapted whole-brain radiotherapy: results of the multicenter Ostdeutsche

Studiengruppe Hamato-Onkologie OSHO-53 phase II study. *Ann Oncol.* 2007 Apr;18(4):665-71. Epub 2006 Dec 21.

31. National Cancer Institute. (a) Adult brain tumors (PDQ[®]): treatment: health professional version. Updated 2010 Jul 8. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/adultbrain/healthprofessional/allpages>
32. National Cancer Institute. (a) Childhood brain stem glioma (PDQ[®]): treatment: health professional version. Updated 2011 May 19. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/child-brain-stem-glioma/healthprofessional/allpages/print>
33. National Cancer Institute. (b) Childhood brain and spinal cord tumors treatment overview (PDQ[®]): health professional version. Updated 2010 Oct 29. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/childbrain/healthprofessional/allpages/print>
34. National Cancer Institute. (b) Childhood central nervous system atypical tetratoid/rhabdoid tumor treatment (PDQ[®]): health professional version. Updated 2011 May 24. Accessed May 25, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/child-CNS-ATRT/healthprofessional>.
35. National Cancer Institute. (c) Childhood central nervous system embryonal tumors treatment (PDQ[®]): health professional version. Updated 2011 May 19. Accessed May 24, 2011. Available at URI address: <http://www.cancer.gov/cancertopics/pdq/treatment/childCNSembryonal/healthprofessional>
36. National Cancer Institute. (d) Childhood astrocytomas treatment (PDQ[®]): health professional version. Updated 2011 May 20. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/child-astrocytomas/HealthProfessional>
37. National Cancer Institute. (e) Childhood craniopharyngioma treatment (PDQ[®]): health professional version. Updated 2011 May 20. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/child-cranio/healthprofessional>
38. National Cancer Institute. (f) Childhood ependymoma treatment (PDQ[®]): health professional version. Updated 2011 May 20. Accessed May 24, 2011. Available at URL address: <http://www.cancer.gov/cancertopics/pdq/treatment/childependymoma/HealthProfessional>
39. National Comprehensive Cancer Network[®] (NCCN) [a]. NCCN GUIDELINES[™] Clinical Guidelines in Oncology[™]. Central nervous system cancers. V2.2011. © National Comprehensive Cancer Network, Inc. 2010, All Rights Reserved. Accessed May 20, 2011. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/cns.pdf
40. Park JE, Kang J, Yoo KH, Sung KW, Koo HH, Lim do H, et al. Efficacy of high-dose chemotherapy and autologous stem cell transplantation in patients with relapsed medulloblastoma: a report on the Korean Society for Pediatric Neuro-Oncology (KSPNO)-S-053 study. *J Korean Med Sci.* 2010 Aug;25(8):1160-6.
41. Perez-Martinez A, Lassaletta A, Gonzalez-Vicent M, Sevilla J, Diaz MA, Madero L. High-dose chemotherapy with autologous stem cell rescue for children with high risk and recurrent medulloblastoma and supratentorial primitive neuroectodermal tumors. *J Neurooncol.* 2005 Jan;71(1):33-8.
42. Ridola V, Grill J, Doz F, Gentet JC, Frappaz D, Raquin MA, et al. High-dose chemotherapy with autologous stem cell rescue followed by posterior fossa irradiation for local medulloblastoma recurrence or progression after conventional chemotherapy. *Cancer.* 2007 Jul 1;110(1):156-63.

43. Shih CS, Hale GA, Gronewald L, Tong X, Laningham FH, Gilger EA, et al. High-dose chemotherapy with autologous stem cell rescue for children with recurrent malignant brain tumors. *Cancer*. 2008 Mar 15;112(6):1345-53.
44. Strother D, Ashley D, Kellie SJ, Patel A, Jones-Wallace D, Thompson S, et al. Feasibility of four consecutive high-dose chemotherapy cycles with stem-cell rescue for patients with newly diagnosed medulloblastoma or supratentorial primitive neuroectodermal tumor after craniospinal radiotherapy: results of a collaborative study. *J Clin Oncol*. 2001 May 15;19(10):2696-704.
45. Sung KW, Yoo KH, Cho EJ, Koo HH, Lim do H, Shin HJ, et al. High-dose chemotherapy and autologous stem cell rescue in children with newly diagnosed high-risk or relapsed medulloblastoma or supratentorial primitive neuroectodermal tumor. *Pediatr Blood Cancer*. 2007 Apr;48(4):408-15.
46. Zachoroulis S, Levy A, Chi SN, Gardner S, Rosenblum M, Miller DC, et al. Outcome for young children newly diagnosed with ependymoma treated with intensive induction chemotherapy followed by myeloablative chemotherapy and autologous stem-cell rescue. *Pediatr Blood Cancer*. 2007 Jul;49(1):34-40.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	7/15/2008	0369	Stem-Cell Transplant for Central Nervous System Tumors

CIGNA, "CIGNA HealthCare" and the "Tree of Life" logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Health and Life Insurance Company, CIGNA Behavioral Health, Inc., CIGNA Health Management, Inc., and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company or CIGNA Health and Life Insurance Company.