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Medical Policy Manual

Topic: Autologous Hematopoietic Stem-Cell Transplantation for Malignant Astrocytomas and Gliomas

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Section: Transplant

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Hematopoietic Stem Cell Transplantation

Hematopoietic stem cell transplantation (HSCT) refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole body radiation therapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from donor (allogeneic HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically "naïve" and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

Preparative Conditioning for HSCT

Autologous HSCT necessitates myeloablative chemotherapy to eradicate cancerous cells from the blood and bone marrow, thus permitting subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic progenitor cells. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who

undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not graft-versus-host disease.

Astrocytomas and Gliomas

Diffuse fibrillary astrocytomas are the most common type of brain tumor in adults. These tumors are classified histologically into 3 grades of malignancy: grade II astrocytoma, grade III anaplastic astrocytoma, and grade IV glioblastoma multiforme. Oligodendrogliomas are diffuse neoplasms that are clinically and biologically most closely related to diffuse fibrillary astrocytomas. However, these tumors generally have better prognoses than diffuse astrocytomas, with mean survival times of 10 years versus 2–3 years. In addition, oligodendrogliomas appear to be more chemosensitive than other types of astrocytomas. Glioblastoma multiforme is the most malignant stage of astrocytoma, with survival times of less than 2 years for most patients.

Treatment of primary brain tumors focuses on surgery, either with curative intent or optimal tumor debulking. Surgery may be followed by radiation therapy and/or chemotherapy. Survival after chemoradiotherapy is largely dependent on the extent of residual tumor after surgical debulking. Therefore, tumors arising in the midline, basal ganglia, or corpus callosum or those arising in the eloquent speech or motor areas of the cortex, which typically cannot be extensively resected, have a particularly poor outcome. Treatment of children younger than 3 years is complicated by the long-term effects of radiation therapy on physical and intellectual function. Therefore, in young children, radiation of the central nervous system (CNS) is avoided whenever possible.

Note: Astrocytomas and gliomas arise from the glial cells. Tumors arising from the neuroepithelium constitute a separate category of malignancies that include CNS neuroblastoma, medulloblastoma, ependymoblastomas, and pinealblastomas. Collectively these tumors may be referred to as primitive neuroectodermal tumors (PNETs). Ependymomas also arise from the neuroepithelium but, because of their more mature histologic appearance, are not considered a member of the PNET family.

MEDICAL POLICY CRITERIA

Autologous HSCT is considered **investigational** as a treatment of the following:

A. Malignant astrocytomas

B. Malignant gliomas, including both glioblastoma multiforme and oligodendroglioma

SCIENTIFIC EVIDENCE[1]

- The 1994 BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessment[2] concluded that the evidence did not demonstrate that autologous hematopoietic stem-cell transplantation (HSCT) improved health outcomes of adult patients with high-grade glial tumors of the brain. The 1999 update of this TEC assessment confirmed these conclusions and noted that although there was much research interest in use of autologous HSCT for glioblastoma multiforme due to its uniformly poor prognosis, the published literature was relatively scant, consisting primarily of single-institution case series. The following representative examples were cited:

- Bouffet and colleagues reported on a series of 22 children and young adults with high-grade gliomas treated with autologous HSCT.[3] The response rate was 29% with 1 complete and 3 partial responses. However, the authors concluded that survival with this procedure was no better than that reported with conventional treatments.
- Heideman and colleagues reported on a case series of 13 pediatric patients with bulky disease or recurrent disease treated with HSCT plus radiotherapy.[4] While the overall response rate was 31%, the authors similarly concluded that overall survival was no better than conventional treatment regimens.
- Finlay and colleagues reported on a 1996 case series of 45 children and young adults with a variety of recurrent central nervous system (CNS) tumors, including gliomas, medulloblastomas, ependymomas, and primitive neuroectodermal tumors.[5] Of the 18 patients with high-grade gliomas, the response rate was 29%. The median survival of this group was 12.7 months. Of the 5 long-term survivors, all had high-grade glioma with minimal residual disease at the time of transplantation. Based in part on these results, the authors recommended aggressive surgical debulking before this procedure is even considered.
- Studies focusing on the use of autologous HSCT in adults with glioblastoma multiforme reported results similar to those in children, being most successful in those with minimal disease at the time of treatment, with an occasional long-term survivor.[6,7]

- A review by Brandes and colleagues concluded that the high drug doses used in this treatment caused excessive toxicity that was not balanced by a significant improvement in survival.[8]
- Levin and co-workers concluded that it was unclear whether autologous HSCT had a role in management of cerebral gliomas.[9]
- Additional reports on small, uncontrolled series of patients with pontine gliomas,[10] recurrent oligodendrogliomas,[11] or those undergoing radiation therapy for high-grade gliomas[12] also did not suggest that this treatment improves survival.
- In a phase II study, Abrey and colleagues evaluated hematopoietic stem-cell transplantation in 39 patients with newly diagnosed oligodendroglioma.[13] The authors reported the median follow-up of surviving patients was 80.5 months, with 78 months progression-free survival. The overall survival median had not been reached, and 18 patients (46%) had relapsed.

A nonrandomized study compared survival outcomes of 27 children (0.4–22 years) with recurrent malignant astrocytomas who underwent myeloablative chemotherapy and autologous HSCT with outcomes in a matched historical cohort (n=56) that received standard chemotherapy regimens following tumor recurrence.[14] Among the 27 children who received myeloablative chemotherapy and autologous HSCT, 5 (18%) succumbed to treatment-related toxicities within about 2 months of transplantation, 17 (63%) had disease progression, while 5 survived and were alive a median of 11 years (range: 8–13 years) after transplantation. Overall survival rates at 4 years were 40 +/- 14% for transplant patients versus 7 +/- 4% with conventional chemotherapy (p=0.018, HR=1.9, 95% CI: 1.1–3.2). The results of this study suggest myeloablative chemotherapy with autologous HSCT can produce long-term survival among children with recurrent malignant astrocytoma. However, lack of a contemporaneous treatment comparison group precludes conclusions as to the relative efficacy of this approach.

Clinical Practice Guidelines

The 2013 National Comprehensive Cancer Network (NCCN) Guidelines on Central Nervous System cancers (v.2.2013) do not list HSCT as a treatment option for patients with astrocytomas or gliomas.[15]

Summary

The data on autologous hematopoietic stem cell transplantation (HSCT) for treatment of malignant astrocytomas and gliomas consists of case series and has not shown survival benefit compared to conventional therapy. Therefore, autologous HSCT is considered investigational.

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CROSS REFERENCES

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Hematopoietic Stem-Cell Transplantation for Miscellaneous Solid Tumors in Adults, Transplant, Policy No. 45.27

Hematopoietic Stem-Cell Transplantation for CNS Embryonal Tumors and Ependymoma, Transplant, Policy No. 45.33

Hematopoietic Stem-Cell Transplantation for Solid Tumors of Childhood, Transplant, Policy No. 45.37

CODES	NUMBER	DESCRIPTION
CPT	38204	Management of recipient hematopoietic cell donor search and cell acquisition
	38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogeneic
	38206	;autologous
	38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
	38208	;thawing of previously frozen harvest, without washing, per donor
	38209	;thawing of previously frozen harvest with washing, per donor
	38210	;specific cell depletion with harvest, T cell depletion
	38211	;tumor cell depletion
	38212	;red blood cell removal
	38213	;platelet depletion
	38214	;plasma (volume) depletion

CODES	NUMBER	DESCRIPTION
	38215	;cell concentration in plasma, mononuclear, or buffy coat layer
	38220	Bone marrow; aspiration only
	38221	Bone marrow; biopsy, needle or trocar
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
	38241	;autologous transplantation
	38242	Allogeneic lymphocyte infusions
	38243	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor, HPC boost
HCPCS	J9000–J9999	Chemotherapy drugs code range
	Q0083–Q0085	Chemotherapy administration code range
	S2140	Cord blood harvesting for transplantation; allogeneic
	S2142	Cord blood derived stem-cell transplantation, allogeneic
	S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)