Autologous Hematopoietic Stem-Cell Transplantation for Malignant Astrocytomas and Gliomas

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Original Effective Date: 04/01/2008
Line(s) of Business: HMO; PPO
Current Effective Date: 10/28/2011
Section: Transplants
Place(s) of Service: Outpatient; Inpatient

I. 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. Bone marrow stem cells may be obtained from the transplant recipient (autologous HSCT) and 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.

Preparative Conditioning for Hematopoietic Stem-Cell Transplantation

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
astrocitoma, and grade IV glioblastoma multiform. 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, respectively. 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 pinealoblastomas. 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. The use of high-dose chemotherapy in tumors arising from the neuroepithelium is addressed separately in another policy.

II. Policy

Autologous hematopoietic stem-cell transplantation is not covered as a treatment of malignant astrocytomas and gliomas. (The latter diagnosis includes both glioblastoma multiforme and oligodendroglioma.)

III. Administrative Guidelines

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>38206</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, autologous</td>
</tr>
<tr>
<td>38208</td>
<td>Thawing of previously frozen harvest</td>
</tr>
<tr>
<td>38209</td>
<td>Washing of harvest</td>
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<tr>
<td>38210</td>
<td>Specific cell depletion with harvest, T-cell depletion</td>
</tr>
<tr>
<td>38211</td>
<td>Tumor-cell depletion</td>
</tr>
<tr>
<td>38212</td>
<td>Red blood cell removal</td>
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<tr>
<td>38213</td>
<td>Platelet depletion</td>
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</tbody>
</table>
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38214 Plasma (volume) depletion
38215 Cell concentration in plasma, mononuclear, or buffy coat layer
38220 Bone marrow, aspiration only
38221 Biopsy, needle or trocar
38241 Bone marrow or blood derived peripheral stem-cell transplantation; autologous

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
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<tbody>
<tr>
<td>Q0083 - Q0085</td>
<td>Chemotherapy, administer code range</td>
</tr>
<tr>
<td>J9000 - J9999</td>
<td>Chemotherapy drug code range</td>
</tr>
<tr>
<td>S2150</td>
<td>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)</td>
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IV. Rationale

An older policy document on use of autologous hematopoietic stem-cell transplantation (HSCT) for this and other malignancies was based on a 1994 TEC Assessment. (1) The Assessment concluded that evidence available at that time did not demonstrate that this procedure improved health outcomes of adult patients with high-grade glial tumors of the brain.

An initial update of the 1994 TEC Assessment reviewed literature published through 1999 and confirmed the Assessment’s conclusions. It 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. (2) 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. (3) 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. (4) 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. (5, 6)

A review by Brandes and colleagues (7) concluded that the high drug doses used in this treatment caused excessive toxicity that was not balanced by a significant improvement in survival. Additional reports on small, uncontrolled series of patients with pontine gliomas, (8) recurrent oligodendrogliomas, (9), or those undergoing radiation therapy for high-grade gliomas (10) also did not suggest that this treatment improves survival. In a Phase I study, Abrey and colleagues evaluated hematopoietic stem-cell transplantation in 39 patients with newly diagnosed oligodendroglioma. (11) 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 (age, 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. (12) Among the 27 children who received myeloablative chemotherapy and autologous HSCT, 5 (18%) succumbed to treatment-related toxicities within approximately 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.

2011 update

An updated literature search in August 2011 identified no controlled studies that would change the conclusions of this policy. Thus, the policy statement is unchanged.

National Cancer Institute Physician Data Query (PDQ) Clinical Trials Database

A search in August 2011 found one active Phase II trial of hematopoietic stem-cell transplantation for newly diagnosed central nervous system tumors, including glioblastoma multiforme and gliosarcoma.

National Comprehensive Cancer Network (NCCN) Guidelines
The 2011 NCCN Guidelines on Central Nervous System Tumors (v.1.2011) do not list HSCT as a treatment option for patients with astrocytomas or gliomas. (13)

V. Important Reminder
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VI. References

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). HDC/AuSCS for high-grade glial tumors of the brain in adults. TEC Assessments 1994; Volume 9, Tab 34.