Hematopoietic Cell Transplantation for Testicular Cancer

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

I. Aetna considers autologous hematopoietic cell transplantation medically necessary for the treatment of persons with testicular cancer who do not attain a complete remission after an initial course of standard-dose chemotherapy, i.e., those with refractory (less than 50 % reduction in tumor burden) testicular cancer or those exhibiting a partial response (at least a 50 % reduction in tumor burden).

II. Aetna considers autologous hematopoietic cell transplantation as consolidation therapy medically necessary for persons with testicular cancer who relapse after an initial course of standard-dose chemotherapy.

III. Aetna considers tandem autologous hematopoietic cell transplantation medically necessary for persons with testicular cancer who have relapsed.
IV. Aetna considers autologous hematopoietic cell transplantation experimental and investigational as initial treatment (i.e., instead of an initial course of standard-dose chemotherapy with Food and Drug Administration-approved drugs) of persons with testicular cancer because the effectiveness of this approach has not been established.

V. Aetna considers allogeneic hematopoietic cell transplantation experimental and investigational for the treatment of persons with testicular cancer because its effectiveness for this indication has not been established.

See also CPB 0352 - Tumor Markers (../300_399/0352.html), and CPB 0532 - Scrotal Ultrasonography (../500_599/0532.html).

Background

Testicular cancer, a highly treatable, commonly curable cancer, accounts for only 1% of all male malignancy. It usually develops in young and middle-age men in the 20- to 40- year old age group. Testicular cancer is one type of germ cell tumors, which can be classified according to their histology, stage, prognosis, or response to chemotherapy. Histology includes seminoma, embryonal carcinoma, teratoma, choriocarcinoma, yolk sac tumor, and mixed germ cell tumors. Seminomas are the most common and can be subdivided into typical, spermatocytic, and anaplastic varieties. All other types of germ cell tumors may be collectively referred to as non-seminomatous germ cell tumors. Seminoma accounts for 40% of all germ cell tumors, while non-seminoma germ cell tumors account for 60%. Testicular palpation is useful in differentiating the type of tumor involved. Seminomas are usually felt throughout the entire testicle, whereas non-seminomas tend to be small hard masses.

Differentiation between seminoma and non-seminoma germ cell tumors is important because the staging, evaluation and management in the two are different. Seminomas are generally characterized by an indolent clinical course, and are more sensitive to radiation therapy than non-seminomas for patients with early-stage disease. Furthermore, seminomas frequently exhibit a predictable pattern of metastatic spread via the regional lymphatics to the retroperitoneal nodes of the abdomen and/or to the mediastinal and supraclavicular lymph nodes before
gaining access to other visceral structures. In contrast, patients with non-seminomas are generally radio-resistant, with pulmonary and other hematogenous metastases more common than for patients with seminomas.

Once the histologic diagnosis is made, the patient must be staged. The stage of the disease is dependent on the location (extent) of the tumor:

- Stage I is limited to the testis, epididymis, or spermatic cord
- Stage II is limited to retroperitoneal (regional) lymph nodes
- Stage III is disease outside the retroperitoneum, involving supradiaphragmatic nodal sites or viscera.

Ultrasonography as well as laboratory tests are used to confirm the diagnosis and stage of disease. In addition to blood cell counts and urine analysis, there are 2 serum tumor markers present in testicular cancer, (i) human chorionic gonadotropin (HCG) and (ii) alpha-fetal protein (AFP). Studies have reported that 40 % of patients diagnosed with disseminated non-seminomas will have an elevated AFP, 75 % will have an elevated HCG, and 85 % will have one or both markers elevated. In contrast, these markers are only present in 10 % of patients with seminoma, although 50 % of patients with stage III seminomas will have elevated HCG levels. Staging is also confirmed by laparotomy and CT scan.

For patients with Stage I disease, radiation therapy (for seminomas) or retroperitoneal lymph node resection (for non-seminomas) has been shown to result in cure rates of greater than 90 %. Additionally, for patients with Stage I non-seminomas, surveillance (after orchiectomy) is another generally accepted alternative. For patients with Stage II, Stage III disease or extragonadal site of origin, treatment with cisplatin-based chemotherapy has been shown to be very effective in achieving a complete remission. The results of treatment of non-seminomatous germ cell tumors have been improved significantly by cisplatin-containing chemotherapy regimens. The literature indicates that first-line therapy generally entails 3 to 4 cycles of the combination regimen of cisplatin, bleomycin, and etoposide. Under established guidelines, patients whose tumors are resistant to cisplatin may proceed to regimens containing carboplatin. Chemotherapy is often followed by surgery to remove residual masses. Regimens used for relapsed disease include cisplatin plus ifosfamide, combined with either etoposide or vinblastine (salvage therapy).
Salvage therapy has been shown to induce long-term complete responses in about 25% of patients with disease that has persisted or recurred following other cisplatin-based regimens. Patients who have had an initial complete response to first-line chemotherapy and those without extensive disease have the most favorable outcome. However, the literature states that few, if any, patients with recurrent non-seminomatous germ cell tumors of extragonadal origin achieve long-term disease-free survival using vinblastine, ifosfamide, and cisplatin if their disease recurred after they received an initial regimen containing etoposide and cisplatin. High-dose chemotherapy with autologous bone marrow transplantation (ABMT) has been used with some success in the setting of refractory disease. Durable complete remissions may be attainable in 10 to 20% of patients with disease resistant to standard cisplatin-based regimens who are treated with high-dose carboplatin and etoposide with ABMT.

A review by Ayash et al (2001) stated that patients with relapsed/refractory testicular cancer benefit most from ABMT if they have platinum-sensitive disease in first relapse. Patients who do poorly despite ABMT have a mediastinal primary site, true cisplatin-refractory disease, disease progression before ABMT, and/or markedly elevated beta-HCG at ABMT. New treatment modalities are needed for the latter group. This observation is in accordance with the view of Flechon and associates (2001) that new strategies are needed to improve the survival rate of poor prognosis germ cell tumor patients.

Yilmaz and associates (2017) noted that about 20 to 25% of the testicular germ cell tumors (TGCT) are relapsed or refractory after first-line therapy and optimal treatment for this group is poorly defined. These investigators analyzed the safety and efficacy of autologous stem cell transplantation (ASCT) in this patient group. A total of 19 patients with 28 ASCT were retrospectively analyzed. All the patients were treated with BEP (bleomycin, etoposide, cisplatin) as first-line therapy and TIP (paclitaxel, ifosfamide, cisplatin) was given as salvage chemotherapy. Stem cell collection was performed with TIP and granulocyte stimulating factor; ASCT was performed with carboplatin (700 mg/m2) and etoposide (750 mg/m2). The results were provided as median (min-max); p < 0.05 was accepted as statistical significant level. After ASCT, complete and partial remission (CR and PR) rates were 47.3% and 31.5%, respectively. The median overall survival (OS) and progression free survival (PFS) were 18 (0 to 37.4 months) and 7 (0 to 15 months) months, respectively. Estimated 2-year OS was 47.4% and PFS was 35.3%. Grade 3/4 toxicities including diarrhea, mucositis, and toxic hepatitis were observed in 5
patients. Only 1 patient died due to complication of transplantation. The authors concluded that although the number of the patients in this study was limited, ASCT appeared to be a safe and effective treatment modality in relapsed refractory non-seminomatous TGCT with an acceptable OS, PFS and mortality rates.

Bin Riaz and colleagues (2018) stated that approximately 20 to 30% of patients with metastatic germ cell cancers (GCCs) can develop relapsed or refractory (RR) disease, about 40 to 50% of patients who relapse after salvage chemotherapy may reach long-term remission. These investigators identified patients who appear to benefit from high-dose chemotherapy (HDCT) and ASCT. To access this, these researchers performed a systematic medical literature review to evaluate the effectiveness of HDCT in the front-line setting, as well as in patients with RR testicular cancer. They searched databases for interventional clinical studies and identified 5,883 studies. They selected 49 studies for inclusion, which included a total of 5,985 patients; 17 studies reported results of newly diagnosed poor-risk GCC patients and 32 studies reported results of RR patients. For newly diagnosed patients with poor prognostic predictors, a risk adjusted strategy using unfavorable tumor marker decline with initial standard chemotherapy regimen and up-front HDCT demonstrated improved outcomes. The authors concluded that these findings suggested a minimum of 2 HDCT cycles with ASCT should be standard of care for patients with RR GCC; failure of HDCT resulted in a poor prognosis with only 10% of patients achieving lasting remission with salvage therapy.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td>38206</td>
<td>Bone marrow or stem cell services/procedures (except allogenic)</td>
</tr>
<tr>
<td>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous transplantation</td>
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<tr>
<td>96401</td>
<td>Chemotherapy administration</td>
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<td></td>
<td>CPT codes not covered for indications listed in the CPB:</td>
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<tr>
<td>38205</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogenic</td>
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<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogenic</td>
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<tr>
<td>38240</td>
<td>Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor</td>
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HCPCS codes covered if selection criteria are met:

<table>
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<tr>
<td>S2150</td>
<td>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 of pre- and post-transplant care in the global definition</td>
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ICD-10 codes covered if selection criteria are met:

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<tr>
<td>C62.00 - C62.92</td>
<td>Malignant neoplasm of testis</td>
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<tr>
<td>D07.69</td>
<td>Carcinoma in situ of other male genital organs [testis]</td>
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The above policy is based on the following references:


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Amendment to
Aetna Clinical Policy Bulletin Number: 0617 Hematopoietic Cell Transplantation for Testicular Cancer

There are no amendments for Medicaid.