Public Statement:

Autologous stem cell transplant is covered for those patients who meet criteria, with authorization through case management by American Health Holding at 877-815-1017 (option 2).

Medical Policy Statement:

High dose chemotherapy with autologous bone marrow, stem cell, or progenitor cell support for the treatment of germ cell tumor of the testicle, ovary, mediastinum or retroperitoneum is considered medically necessary and is covered:

- For incomplete remission following standard chemotherapy:
- For consolidation following second complete remission induced by standard chemotherapy;
- Following second relapse to standard chemotherapy.

Limits:

High dose chemotherapy with allogeneic stem and/or progenitor cell support is not covered following autologous stem and/or progenitor cell transplantation.
Tandem high dose chemotherapy with autologous stem and/or progenitor cell support is not covered for any diseases other than multiple myeloma and Waldenstrom’s macroglobulinemia.

A second or subsequent course of high dose chemotherapy with allogeneic or autologous stem cell and/or progenitor cell support for treatment of relapsed disease is covered only for patients who have shown a complete response to the initial high dose chemotherapy/transplant regimen.

Coverage of high dose chemotherapy with allogeneic or autologous stem and/or progenitor cell support for a patient with two active malignant diseases is covered only if both diseases have a specific coverage policy and the patient meets all criteria for both high dose chemotherapy with stem and/or progenitor cell treatment regimens.

**Background:**

Germ cell tumors comprise the vast majority of primary testicular neoplasms, although germ cell tumors can arise in the ovary and in extragonadal locations, such as in the retroperitoneum or mediastinum. Germ cell tumors can be classified according to their histology, stage, prognosis, or response to chemotherapy.

Histologies include seminoma, embryonal carcinoma, teratoma, choriocarcinoma, yolk DAC tumor, and mixed germ cell tumors. Seminomas are the most common; all other types of germ cell tumors may be collectively referred to as non-seminomatous germ cell tumors.

The stage is dependent of the location of the tumor. In terms of testicular tumor, Stage I is limited to the testis, Stage II is disease spread to the retroperitoneum, and Stage III disease is distant (supradiaphragmatic) disease.

Prognostic classifications systems take into account the site of the primary tumor (testis versus extragonadal), tumor marker levels, and site of visceral disease. Therapy is often dictated by the prognosis. For example, first line therapy for good and intermediate risk patients is usually 3 or 4 cycles of the combination regimen of cisplatin, bleomycin and etoposide. Second line therapy often consists of combined therapy with vinblastine, ifosfamide, and cisplatin. 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 either with etoposide or vinblastine. The probability of long-term continuous complete response diminishes with each successive relapse.

The term partial response is defined as at least a 50% reduction in tumor burden.
The term refractory is defined as a less than 50% reduction in tumor burden. Therefore, even those tumors that exhibited a 50% reduction in tumor burden, for example, would be considered refractory. Tumor response can be measured using serial CT scans, or levels of circulating tumor markers, such as alpha fetoprotein.

Randomized controlled trials have failed show any benefit of high dose chemotherapy – autologous stem cell support versus standard platinum based chemotherapy for initial treatment of metastatic germ cell tumor. Single cycle high dose chemotherapy – autologous stem cell support versus standard salvage chemotherapy also failed to show any benefit as salvage therapy for patients failing first-line platinum chemotherapy for advanced germ cell tumors. Despite the findings in the latter study, a large retrospective case series of patients who failed first line therapy did demonstrate significant improved survival following 2-cycle high dose chemotherapy - stem cell support.

Agarwal and colleagues reported their experience at Stanford in treating 37 consecutive patients who received high-dose chemotherapy and autologous HSCT between 1995 and 2005 for relapsed germ-cell tumors (Agarwal, 2009). The median patient age was 28 years, with 34 males and 3 females. Primary tumor sites included 24 testes/adnexal, 10 chest/neck/retroperitoneal, and 3 central nervous system. Twenty-nine of the patients had received prior standard salvage chemotherapy. Three year overall survival was 57% and 3 year progression-free survival was 49%.

In 2005, Pico and colleagues reported on a randomized trial comparing 4 cycles of conventional-dose chemotherapy to 3 cycles of the same regimen followed by carboplatin-based high-dose chemotherapy plus autologous HSCT in 280 patients who had relapsed after a complete or partial remission following first-line therapy with a cisplatin-based regimen (Pico, 2005). However, high-dose chemotherapy in the experimental arm followed 3 cycles of conventional-dose chemotherapy, which differs from most current practice in the U.S., where a single cycle is used prior to high-dose chemotherapy. As a consequence, 38 of 135 (28%) randomized to the high-dose chemotherapy arm did not receive high-dose chemotherapy because of progression, toxicity, or withdrawal of consent.

**National Comprehensive Cancer Network (NCCN) Guidelines**

The 2010 (v.1.2010) NCCN guidelines for the treatment of testicular cancer state that if a patient with favorable prognostic factors (defined as testicular primary site, prior complete response to first line therapy, low levels of serum markers and low volume disease), experiences an incomplete response to conventional-dose salvage chemotherapy therapy or relapses after salvage chemotherapy, high-dose chemotherapy with autologous stem cell support is the preferred option. Patients with unfavorable prognostic factors for conventional-dose salvage therapy (e.g. an incomplete response to first line therapy) and patients requiring third-line salvage therapy are considered for treatment with high-dose chemotherapy plus autologous stem cell support (category 2B). The guidelines do not address the use of tandem or sequential HSCT in the treatment of testicular tumors.
References:


High-dose chemotherapy plus allogeneic stem cells to treat chronic lymphocytic leukemia or small lymphocytic lymphoma. 2002 Blue Cross Blue Shield Association Technology Evaluation Center Assessment.


Application to Products

This policy applies to ARBenefits. Consult ARBenefits Summary Plan Description (SPD) for additional information.

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