



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 Epithelial Ovarian Cancer

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Hyperlink to Related Coverage Policies

Genetic Testing for Susceptibility to Breast and Ovarian Cancer (e.g., BRCA1 and BRCA2)

Prophylactic Oophorectomy or Salpingo-oophorectomy With or Without Hysterectomy

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Coverage Policy

CIGNA does not cover autologous or allogeneic hematopoietic stem-cell transplantation (HSCT) for the treatment of epithelial ovarian cancer because each is considered experimental, investigational or unproven.

General Background

Ovarian cancer represents tumors of epithelial, germ cell, or sex cord–stromal origin. In general, ovarian tumors are classified according to the kind of cells from which the tumor originated and whether the tumor is benign or cancerous. Identification of the type of cancer is important for treatment and prognosis, as is the stage and grade of tumor. Approximately 90% of ovarian cancer is epithelial in origin and typically occurs in postmenopausal women.

The diagnosis of epithelial ovarian cancer presents significant treatment challenges due to the advanced stage of most patients with this disease (Cannistra, 2008). According to the National Cancer Institute [NCI], (2010a) factors indicative of a more favorable prognosis include younger age, good performance status, cell type other than mucinous and clear cell, lower stage, well-differentiated tumor, smaller disease volume prior to surgical debulking, absence of ascites, and smaller residual tumor following primary cytoreductive surgery.

Treatment Options

The National Cancer Institute (NCI, 2010a; 2010b) and the National Comprehensive Cancer Network® ([NCCN®], 2010) have defined treatment options for epithelial ovarian cancer. These include surgical staging with cytoreduction, systemic chemotherapy, and intraperitoneal chemotherapy for select patients with optimally cytoreduced disease. Patients with any stage of ovarian cancer are appropriate candidates for clinical trials (NCI, 2010a).

Epithelial ovarian cancer demonstrates a high response rate to standard-dose chemotherapy and several clinical studies have identified a relationship between dose intensity and response. The use of high-dose chemotherapy with stem-cell transplantation (HSCT) has been proposed based on the hypothesis that major dose escalations within the myeloablative range are needed to overcome tumor cell resistance and produce a meaningful clinical improvement.

Stem-Cell Transplantation

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a patient. HSCs are immature cells that can develop into any of the three types of blood cells (red cells, white cells or platelets). Hematopoietic stem-cell transplantation (HSCT) can be either autologous (i.e., using the patient's stem cells) or allogeneic (i.e., using stem cells from a donor).

High-Dose Chemotherapy and Autologous HSCT: The use of high-dose chemotherapy (HDC) with autologous HSCT for the treatment of epithelial ovarian cancer remains controversial (Armstrong, 2008; Papadimitriou, 2007). The effectiveness of single or sequential HDC with autologous HSCT has not been proven in several randomized controlled clinical trials (RCT) (Papadimitriou, 2007; Mobus, 2007; Goncalves, 2006; Stiff, 2004) or retrospective comparison of outcomes achieved with HDC compared with standard dose therapy (Stiff, 2000).

Papadimitriou et al. (2007) compared the effectiveness and tolerability of HDC and autologous HSCT as a consolidation approach in women with chemosensitive advanced epithelial ovarian cancer. Eighty patients who achieved their first complete remission after six cycles of standard dose chemotherapy were randomly assigned to receive high-dose melphalan or other treatment. Patients not assigned to the high-dose arm were considered the control arm. Of the 37 patients assigned to receive the high-dose therapy, eleven patients (29%) did not receive high-dose therapy. In an intent-to-treat analysis, there were no significant differences between the two arms in time to progression ($p=0.59$) or overall survival ($p=0.38$). The use of high-dose chemotherapy failed to yield a statistically significant improvement in outcome.

In another RCT involving 58 women with stage III or stage IV persistent or recurrent ovarian cancer, participants were assigned to receive one of two high-dose chemotherapy treatment regimens; both were followed by autologous HSCT. No significant differences were noted in overall or progression-free survival rates between regimens (Stiff, 2004).

In other studies, limited by uncontrolled design and/or small participant populations, high response rates were noted; however, response rates and survival durations were short (Armstrong, 2008; Bengala, 2005; Donato, 2004). Additionally, in a prospective trial by Schilder et al. (2003), individuals with advanced ovarian cancer who had undergone surgical treatment but had not had previous chemotherapy received high-dose chemotherapy (HDC) followed by autologous hematopoietic stem-cell transplantation (HSCT). Complete response rates were low (12.5%); 11 of 45 cycles of the protocol therapy resulted in hospitalizations. High treatment-related morbidity and low efficacy of the therapy did not support continuing, and the study was closed early.

Sequential High-Dose Chemotherapy (HDC) and Autologous HSCT: Sequential cycles of HDC followed by autologous HSCT have also been proposed for the treatment of individuals with stage III and IV epithelial ovarian cancer. Sequential HDC involves performing multiple cycles of chemotherapy followed by a single HSCT. This therapy potentially allows an increase in the total dose of chemotherapy that can be given; however, some patients are unable to tolerate the side effects of the chemotherapy cycle and transplantation process and are therefore unable to complete multiple cycles.

The outcomes achieved in an RCT as well as several case series do not support a clear advantage of sequential HDC and autologous HSCT compared with conventional dose chemotherapy alone (Mobus, 2007; Goncalves, 2006; Ikeba, 2004; Viret, 2002; Boiko, 2001; Prince, 2001; Schilder, 2001).

Summary for Autologous Hematopoietic Stem-Cell Transplantation (HSCT)

To date the effectiveness of single or sequential high-dose chemotherapy (HDC) followed by autologous HSCT for the treatment of epithelial ovarian cancer has not been demonstrated. Compared with conventional dose chemotherapy, the use of HDC and autologous HSCT has not resulted in improved overall survival. The role of this therapy has not yet been established for this indication; however, it remains an area of clinical investigation.

Allogeneic HSCT: In theory, the graft-versus-tumor effect from allogeneic HSCT may cause regression of disease in patients with solid organ cancers; however, there is scarce data in the published, peer-reviewed scientific literature regarding the use of allogeneic HSCT for epithelial ovarian cancer. Studies are limited to small-case series and retrospective analyses. Patient selection has primarily targeted patients with advanced refractory disease who have exhausted all other options, including previous treatment with high-dose chemotherapy with autologous HSCT. Reported outcomes include slow disease regression followed by disease relapse in a majority of patients (Bay, 2010; Donato, 2004; Hanel, 2003). The safety and effectiveness of allogeneic HSCT has not yet been supported by solid clinical evidence. At this time the role of allogeneic HSCT has not been established for this indication.

Professional Societies/Organizations

National Cancer Institute (NCI): The NCI (2010) notes that high-dose chemotherapy with hematopoietic stem cell support does not result in improved survival in stage III or stage IV epithelial ovarian cancer.

National Comprehensive Cancer Network Guidelines™ (NCCN Guidelines™): Practice Guidelines in Oncology for Ovarian Cancer (2010) note that regarding epithelial ovarian cancer, panel members discussed the issue of dose intensification utilizing high-dose chemotherapy with peripheral blood stem cell transplantation in selected patients with previously untreated ovarian cancer, or as a consolidation strategy after induction therapy with standard drug doses. The Guidelines note that “The consensus of the panel is that this approach remains investigational and should not be performed outside of an approved clinical trial.”

Summary

There is insufficient evidence in the published, peer-reviewed scientific literature to support the safety and effectiveness of autologous or allogeneic hematopoietic stem-cell transplantation (HSCT) for the treatment of epithelial ovarian cancer.

Coding/Billing Information

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

Experimental/Investigational/Unproven/Not Covered:

| CPT®* Codes | Description |
|-------------|--|
| 38205 | Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic |
| 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 |
| 38210 | Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion |
| 38211 | Transplant preparation of hematopoietic progenitor cells; tumor cell depletion |
| 38212 | Transplant preparation of hematopoietic progenitor cells; red blood cell removal |
| 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 |
| 38240 | Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic |
| 38241 | Bone marrow or blood-derived peripheral stem cell transplantation; autologous |
| 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 |
| 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 |
|---------------------------------|--|
| 183.0 | Malignant neoplasm of ovary and other uterine adnexa; ovary |
| 198.6 | Secondary malignant neoplasm of other specified sites; ovary |

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

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Policy History

| Pre-Merger Organizations | Last Review Date | Policy Number | Title |
|---------------------------------|-------------------------|----------------------|--|
| CIGNA HealthCare | 4/15/2008 | 0321 | Stem-Cell Transplant for Epithelial Ovarian Cancer |

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