Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer

Policy # 00054
Original Effective Date: 01/28/2002
Current Effective Date: 07/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults is addressed separately in medical policy 00059.

Note: Hematopoietic Cell Transplantation in the Treatment of Germ-Cell Tumors is addressed separately in medical policy 00056.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers autologous and allogeneic hematopoietic cell transplantation to treat advanced stage epithelial ovarian cancer to be **investigational.***

Background/Overview

Epithelial Ovarian Cancer

Several types of malignancies can arise in the ovary; epithelial carcinoma is the most common. Epithelial ovarian cancer is the fifth most common cause of cancer death in women. New cases and deaths from ovarian cancer in the United States for 2023 were estimated at 19,710 and 13,270, respectively. Most ovarian cancer patients present with widespread disease, and the National Cancer Institute Surveillance, Epidemiology and Results Program reported a 50.8% 5-year survival for all cases between 2013 and 2019.

Treatment

Current management for advanced epithelial ovarian cancer is cytoreductive surgery with chemotherapy. Approximately 75% of patients present with International Federation of Gynecology and Obstetrics stage III to IV ovarian cancer and are treated with paclitaxel plus a platinum analogue

(e.g. cisplatin), the preferred regimen for the newly diagnosed advanced disease. Use of platinum and taxanes has improved progression-free survival and overall survival in advanced disease to between 16 and 21 months and 32 and 57 months, respectively. However, cancer recurs in most women, and they die of the disease because chemotherapy drug resistance leads to uncontrolled cancer growth.

Hematopoietic Cell Transplantation
HCT is a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of drugs with or without whole body radiotherapy. Bone marrow stem cells may be obtained from the transplant recipient (autologous HCT) or a 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 "naive" and thus are associated with a lower incidence of rejection or graft-versus-host disease.

HCT is an established treatment for certain hematologic malignancies; however, its use in solid tumors in adults is largely experimental.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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The use of hematopoietic cell transplantation (HCT) has been investigated to treat patients with epithelial ovarian cancer. Hematopoietic stem cells are infused to restore bone marrow function after cytotoxic doses of chemotherapeutic agents with or without whole body radiotherapy.

Summary of Evidence
For individuals who have advanced-stage epithelial ovarian cancer who receive HCT, the evidence includes randomized trials and data from case series and registries. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related mortality and morbidity. Although some observational studies have reported longer survival in subsets of women with advanced epithelial ovarian cancer than in women treated with standard chemotherapy, none of the randomized trial evidence has shown a benefit from HCT in this population. Overall, the evidence has not shown that HCT improves health outcomes in treating epithelial ovarian cancer, including survival, compared with conventional standard doses of chemotherapy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in ‘Supplemental Information if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network
Current National Comprehensive Cancer Network (NCCN) guidelines on epithelial ovarian cancer including fallopian tube cancer and primary peritoneal cancer (v.2.2023) do not address hematopoietic cell transplantation (HCT) for epithelial ovarian cancer for patients either with newly diagnosed or with relapsed or refractory disease. However, use of high-dose chemotherapy with HCT received a category 2B recommendation for individuals with certain malignant germ cell tumors demonstrating abnormal tumor markers and definitive recurrent disease and a category 2A recommendation in those with persistently elevated markers and definitive residual disease. NCCN notes that "patients with potentially curable recurrent germ cell disease should be referred to a tertiary care institution for HCT consultation and potentially curative therapy."

Accordingly, NCCN guidelines on HCT (v.3.2023) only reference ovarian germ cell tumors as an indication for HCT.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
The Centers for Medicare & Medicaid Services currently have the following national noncoverage decision on autologous stem cell transplantation (AuSCT): "Insufficient data exist to establish definite conclusions regarding the efficacy of AuSCT for the following condition[s]: Solid tumors (other than neuroblastoma)."

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in December 2023 did not identify any ongoing or unpublished trials that would likely influence this review.

References

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2. National Cancer Institute, Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Ovarian Cancer. n.d.; https://seer.cancer.gov/statfacts/html/ovary.html.
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11. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation (HCT). Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf.
12. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation (110.23, formerly 110.8.1). 2016: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366.

Policy History

Original Effective Date: 01/28/2002
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12/06/2001	Medical Policy Committee review.
01/28/2002	Managed Care Advisory Council approval.
05/07/2004	Medical Director Review
05/18/2004	Medical Policy Committee review. High-Dose Chemotherapy and Hematopoietic Stem Cell Support for treatment of ovarian epithelial cancer policy developed separately from current HDC with Hematopoietic Stem Cell Support policy. Format revision. No substance change to policy.
06/28/2004	Managed Care Advisory Council approval

07/07/2006	Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
08/02/2006	Medical Director Review
08/09/2006	Medical Policy Committee approval
08/06/2008	Medical Director Review
08/20/2008	Medical Policy Committee approval. No change to coverage eligibility.
08/06/2009	Medical Policy Committee approval
08/26/2009	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Title changed.
12/01/2010	Medical Policy Committee approval
12/15/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2013	Coding update
12/12/2013	Medical Policy Committee review
12/18/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2015	Medical Policy Committee review
06/17/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
06/02/2016	Medical Policy Committee review
06/20/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
06/01/2017	Medical Policy Committee review
06/21/2017	Medical Policy Implementation Committee approval. Removed the word “Stem” from title and policy.

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11/15/2017	Coding update
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. Added "advanced stage" to investigational statement.
06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/03/2021	Medical Policy Committee review
06/09/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2022	Medical Policy Committee review
06/08/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/01/2023	Medical Policy Committee review
06/14/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/06/2024	Medical Policy Committee review
06/12/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 06/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38230, 38240, 38241, 38242, 38243
HCPCS	S2140, S2142, S2150
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or

diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.