MEDICAL POLICY

POLICY TITLE	HEMATOPOIETIC CELL TRANSPLANTATION FOR MISCELLANEOUS SOLID TUMORS IN ADULTS
POLICY NUMBER	MP 9.048

Effective Date:	6/1/2023

I. POLICY

Autologous or allogeneic hematopoietic cell transplant is considered **investigational** for the following malignancies in adults. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

- Lung cancer, and histology
- Colon cancer
- Rectal cancer
- Pancreatic cancer
- Stomach cancer
- Esophageal cancer
- Gall bladder cancer
- Cancer of the bile duct
- Renal cell cancer
- Cervical cancer
- Uterine cancer
- Cancer of the fallopian tubes
- Prostate cancer
- Nasopharyngeal cancer
- Paranasal sinus cancer
- Neuroendocrine tumors
- Soft tissue sarcomas
- Thyroid tumors
- Tumors of the thymus
- Tumors of unknown primary origin
- Malignant melanoma

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat and manage patients with cancer. Guidelines evolve continuously as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

Cross-references:

MP 9.001 Placental/Umbilical Cord Blood as a Source of Stem Cells.

MP 9.047 Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer
MP 9.050 Hematopoietic Cell Transplantation for CNS Embryonal Tumors and Ependymoma
MP 9.054 Hematopoietic Cell Transplantation for Solid Tumors of Childhood
MP 9.052 Hematopoietic Cell Transplantation in the Treatment of Germ-Cell Tumors

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:
https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND

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Hematopoietic cell transplantation (HCT) is an established treatment for certain hematologic malignancies and has been investigated for a variety of adult solid tumors. Interest continues in exploring nonmyeloablative allogeneic HCT (allo-HCT) for a graft-versus-tumor effect of donor-derived T-cells in metastatic solid tumors.

HEMATOPOIETIC CELL TRANSPLANTATION

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 cytotoxic drugs with or without whole body radiotherapy. Approximately 20,000 hematopoietic cell transplantation (HCT) procedures are performed in the United States annually. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or from umbilical cord blood shortly after delivery of neonates. Cord blood is discussed in detail in MP-9.001.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR

(antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

Conditioning for HCT

Conventional Conditioning

The conventional ("classical") practice of allo-HCT involves the administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs. Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease (GVHD), which increases susceptibility to opportunistic infections

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allo-HCT

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism. In this review, the term RIC will refer to all conditioning regimens intended to be nonmyeloablative.

HCT IN SOLID TUMORS IN ADULTS

HCT is an established treatment for certain hematologic malignancies. Its use in solid tumors is less well established, although it has been investigated for a variety of solid tumors. With the

advent of nonmyeloablative allogeneic transplant, interest has shifted to exploring the generation of alloreactivity to metastatic solid tumors via a graft-versus-tumor effect of donor-derived T cells.

HCT as a treatment for ovarian cancer, germ cell tumors, ependymoma, or malignant glioma is addressed separately. HCT as a treatment for breast cancer is not addressed. This medical policy collectively addresses other solid tumors of adults for which HCT has been investigated, including lung cancer, malignant melanoma, tumors of the gastrointestinal tract (affecting the colon, rectum, pancreas, stomach, esophagus, gallbladder, or bile duct), male and female genitourinary systems (e.g., renal cell carcinoma, prostate cancer, cervical cancer, uterine cancer, fallopian tube cancer), tumors of the head and neck, soft tissue sarcoma, thyroid tumors, tumors of the thymus, and tumors of unknown primary origin.

Current National Comprehensive Cancer Network guidelines on the tumors addressed in this policy do not discuss hematopoietic cell transplantation (HCT) as a treatment option.

REGULATORY STATUS

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.

IV. RATIONALE

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SUMMARY OF EVIDENCE

Autologous HCT

For individuals who have adult soft tissue sarcomas who receive autologous HCT, the evidence includes 2 randomized controlled trials (RCTs), a number of phase 2 single-arm studies (some of which have been summarized in a systematic review), and a retrospective registry study. Relevant outcomes are overall survival (OS), disease-specific survival, and treatment-related mortality and morbidity. Although a small phase 2 RCT reported longer survival for patients treated with autologous HCT than with standard chemotherapy, this trial did not show a survival benefit with HCT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have small cell lung cancer who receive autologous HCT, the evidence includes several RCTs and systematic reviews of these studies. Relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. Studies have not reported increased OS for patients with small-cell lung cancer treated with autologous HCT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Allogeneic-HCT

For individuals who have renal cell carcinoma, colorectal cancer, pancreatic cancer, or nasopharyngeal cancer who receive allo-HCT, the evidence includes small single-arm series.

Relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. The evidence for allo-HCT to treat renal cell carcinoma, colorectal cancer, pancreatic cancer, and nasopharyngeal cancer has been limited to small case series. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

V. DEFINITIONS

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NA

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice, and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Considered investigational when used for treatment of miscellaneous solid tumors listed; therefore not covered:

Procedure Codes								
S2142	S2150	38204	38205	38206	38207	38208	38209	38210
38211	38212	38213	38214	38215	38230	38232	38240	38241
38242								

IX. REFERENCES

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X. POLICY HISTORY

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MP 9.048	**CAC 5/20/14 Minor**. Information on HSCT for Miscellaneous Solid Tumors in Adults was extracted from MP 9.037 Autologous and Allogeneic Stem Cell Transplantation (which was retired) and this new separate policy created. No change to policy statements. References updated. Policy rationale section added. Policy coded.
	CAC 6/2/15 Consensus review. No change to policy statements. References and rationale updated**.** Codes reviewed.
	CAC 5/31/16 Consensus review. No change to policy statements. References and rationale updated. Coding reviewed.
	Admin update 1/1/17: Product variation section reformatted.

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	CAC 7/25/17 Consensus review. Policy statement unchanged. Changed "hematopoietic stem cell transplantation" to "hematopoietic cell transplantation" per NCCN terminology change. Coding Reviewed
	1/1/18 Admin update. Medicare variations removed from Commercial Policies. Coding reviewed.
	4/04/18 Consensus review. Administrative language change, "hematopoietic stem cell transplant" now "hematopoietic cell transplant." Description/Background, Rationale, and Reference sections updated.
	2/25/19 Consensus review. No change to the policy statements. References reviewed.
	02/27/20 Consensus review. No change to the policy statements. References reviewed.
	2/5/21 Consensus review. No change to policy statement. Code 38207 added. Background and rationale updated. References updated.
	2/17/22 Consensus review. NCCN statement added, no changes to current criteria. References updated.
	2/27/23 Consensus review. No changes to policy statement. Updated background and references.

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