MEDICAL POLICY

POLICY TITLE	**HEMATOPOIETIC CELL TRANSPLANTATION FOR CHRONIC MYELOID LEUKEMIA**
POLICY NUMBER	**MP 9.039**

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective date:	**5/1/2026**

POLICY

Allogeneic hematopoietic cell transplantation (HCT) using a myeloablative conditioning regimen may be considered **medically necessary** as a treatment of chronic myeloid leukemia.

Allogeneic HCT using a reduced-intensity conditioning regimen may be considered **medically necessary** as a treatment of chronic myeloid leukemia in individuals who meet clinical criteria for an allogeneic HCT but who are not considered candidates for a myeloablative conditioning allogeneic HCT.

Autologous HCT is **investigational** as a treatment of chronic myeloid leukemia. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Policy Guidelines

Some individuals for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced intensity conditioning allogeneic HCT. These include those individuals whose age (typically greater than 60 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status score) preclude use of a standard myeloablative conditioning regimen.

For individuals who qualify for a myeloablative allogeneic HCT on the basis of clinical status, either a myeloablative or reduced-intensity conditioning regimen may be considered medically necessary.

Cross-References:
MP 9.001 Placental/Umbilical Cord Blood as a Source of Stem Cells
MP 9.038 Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma
MP 9.040 Hematopoietic Cell Transplantation for Acute Myeloid Leukemia
MP 9.041 Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia
MP 9.042 Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas
MP 9.043 Hematopoietic Cell Transplantation for Hodgkin Lymphoma

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MP 9.044 Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome
MP 9.045 Hematopoietic Cell Transplantation for Primary Amyloidosis
MP 9.046 Hematopoietic Cell Transplantation for Waldenstrom Macroglobulinemia
MP 9.047 Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer
MP 9.048 Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults
MP 9.050 Hematopoietic Cell Transplantation for CNS Embryonal Tumors and Ependymoma
MP 9.052 Hematopoietic Cell Transplantation in the Treatment of Germ-Cell Tumors
MP 9.053 Hematopoietic Cell Transplantation for Autoimmune Diseases
MP 9.054 Hematopoietic Cell Transplantation for Solid Tumors of Childhood
MP 9.055 Allogeneic Hematopoietic Cell Transplantation for Genetic Diseases and Acquired Anemias
MP 9.056 Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms

PRODUCT VARIATIONS

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

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

DESCRIPTION/BACKGROUND

CHRONIC MYELOID LEUKEMIA

Chronic myeloid leukemia (CML) is a hematopoietic stem cell disorder characterized by the presence of a chromosomal abnormality called the Philadelphia chromosome, which results from a reciprocal translocation between the long arms of chromosomes 9 and 22. This cytogenetic change results in constitutive activation of the fusion gene BCR-ABL, a tyrosine kinase that stimulates unregulated cell proliferation, inhibits cell apoptosis, creates genetic instability, and upsets interactions between CML cells and the bone marrow stroma only in malignant cells. The disease accounts for about 15% of newly diagnosed cases of leukemia in adults and occurs in 1 to 2 cases per 100,000 adults.

The natural history of the disease consists of an initial (indolent) chronic phase, lasting a median of 3 years, which typically transforms into an accelerated phase, followed by a “blast crisis,” which is usually the terminal event. Most patients present in chronic phase, often with nonspecific symptoms secondary to anemia and splenomegaly. A diagnosis is based on the presence of the Philadelphia chromosome abnormality by routine cytogenetics, or by detection of abnormal BCR-ABL products by fluorescence in situ hybridization or molecular studies, in the setting of persistent unexplained leukocytosis. Conventional-dose chemotherapy regimens used

for chronic phase disease can induce multiple remissions and delay the onset of blast crisis to a median of 4 to 6 years. However, successive remissions are invariably shorter and more difficult to achieve than their predecessors.

Treatment

Historically, the only curative therapy for CML in blast phase has been allogeneic hematopoietic cell transplantation (allo-HCT), which was used more widely earlier in the disease process given the lack of other therapies for chronic phase CML. Drug therapies for chronic phase CML were limited to nonspecific agents including busulfan, hydroxyurea, and interferon-α.

Imatinib mesylate (Gleevec®), a selective inhibitor of the abnormal BCR-ABL tyrosine kinase protein, is considered the treatment of choice for newly diagnosed CML. While imatinib can be highly effective in suppressing CML, it is not curative and is ineffective in 20% to 30% of patients, initially or due to development of *BCR-ABL* variants that cause resistance to the drug. Even so, the overall survival of patients who present in chronic phase is greater than 95% at 2 years and 80% to 90% at 5 years.

For CML, two other tyrosine kinase inhibitors ([TKIs]; dasatinib, nilotinib) have received marketing approval from the U.S. Food and Drug Administration (FDA) as first-line therapies or following failure or patient intolerance of imatinib. Three additional TKIs (bosutinib, ponatinib, asciminib) have been approved for use in patients resistant or intolerant to prior therapy.

For patients on imatinib who have disease progression, the therapeutic options include increasing the imatinib dose, changing to another TKI, or allo-HCT. Detection of *BCR-ABL* variants may be important in determining an alternative TKI; the presence of the *T315I* variant is associated with resistance to all TKIs and should indicate the need for allo-HCT or experimental therapy. TKIs have been associated with long-term remissions; however, if disease progression occurs on TKI therapy, allo-HCT is generally indicated and offers the potential for cure.

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allo-HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Cord blood is discussed in detail in medical policy 9.001, Placental/Umbilical Cord Blood as a Source of Stem Cells.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allo-HCT, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLAs) 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.

Conventional Conditioning for HCT

The conventional ("classical") practice of allo-HCT involves 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 initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect mediated by non-self-immunologic effector cells. While the slower GVM 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 and 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 also increase susceptibility to opportunistic infections.

The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow 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 clinical 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 GVM 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 *reduced-intensity conditioning* will refer to all conditioning regimens intended to be nonmyeloablative.

REGULATORY STATUS

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

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RATIONALE

SUMMARY OF EVIDENCE

For individuals who have CML who receive allo-HCT, the evidence includes systematic reviews, randomized controlled trials (RCTs), and multiple prospective and retrospective series. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The introduction of TKIs has significantly changed the clinical use of HCT for CML. TKIs have replaced HCT as initial therapy for patients with chronic phase CML. However, a significant proportion of cases fail to respond to TKIs, develop a resistance to them, or cannot tolerate TKIs and proceed to allo-HCT. Also, allo-HCT represents the only potentially curative option for those patients in the accelerated or blast phase CML. Currently, available evidence has suggested that TKI pretreatment does not lead to worse outcomes if HCT is needed. Myeloablative conditioning regimens before HCT are used in younger (less than 60 years of age) patients without significant comorbidities. However, for patients with more comorbidities and/or more advanced age for whom myeloablative conditioning regimens would be prohibitively high-risk, evidence has suggested that reasonable outcomes can be obtained after HCT. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have CML who receive autologous HCT, the evidence includes case series. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. In the largest series (n=200 patients), median survival was 36 months for patients transplanted during an accelerated phase; median survival data were not available for patients transplanted in chronic phase. Controlled studies are needed to permit conclusions on the impact of autologous HCT on health outcomes in patients with CML. The evidence is insufficient to determine the effects of the technology on health outcomes.

DEFINITIONS

KARNOFSKY PERFORMANCE STATUS is a standard way of measuring the ability of cancer patients to perform ordinary tasks where the score ranges from 0 to 100. A higher score means the patient is better able to carry out daily activities.

MYELOABLATIVE CONDITIONING REGIMEN is a strong treatment given before a stem cell transplant that uses high-dose chemotherapy and/or radiation to destroy the bone marrow and immune system. This approach aims to ensure the transplanted stem cells can engraft successfully and helps to prevent rejection.

DISCLAIMER

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as permitted by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit

program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

CODING INFORMATION

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.

Investigational; therefore, not covered:

Procedure Codes							
38206	38232	38241					

Covered when medically necessary:

Procedure Codes								
38204	38205	38207	38208	38209	38210	38211	38212	38213
38214	38215	38230	38240	S2140	S2142	S2150		

ICD-10-CM Diagnosis Codes	Description
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse

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POLICY HISTORY

MP 9.039	**04/09/2020 Consensus Review**. Policy criteria unchanged, minor revisions under Description/Background section, references updated. Coding reviewed.
	05/26/2021 Consensus Review. Policy unchanged references and coding reviewed.
	02/08/2022 Consensus Review. NCCN statement added, no changes to current criteria. No references added.
	02/03/2023 Consensus Review. No changes to policy statement. References reviewed and updated. Coding reviewed.
	02/26/2024 Consensus Review. Updated references. No change to coding.
	11/19/2024 Administrative Update. Removed NCCN statement.
	01/16/2025 Consensus Review. No changes to policy statement. Coding reviewed.
	01/15/2026 Consensus Review. No changes to policy statement. Removed benefit variations. Updated policy formatting, cross-references, product variations, background, definitions, disclaimer, and references. No coding changes.