Molina Clinical Policy
Hematopoietic Stem Cell Transplantation for Chronic Myelogenous Leukemia (CML): Policy No. 187

Last Approval: 4/10/2024
Next Review Due By: June 2024

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Chronic Myelogenous Leukemia (CML or chronic granulocytic leukemia or chronic myeloid leukemia) is a disease of both the bone marrow and blood. It most often occurs in middle-aged adults. CML is characterized by the fact that too many granulocytes (neutrophils, eosinophils, and basophils) and not enough red blood cells and platelets develop from bone marrow myeloid stem cells. This can lead to anemia, infection, and increased bleeding from abrasions. Signs and symptoms of CML may include night sweats, fever, exhaustion, and weight loss. It is thought that CML is due to a non-inherited genetic mutation called the “Philadelphia chromosome.” The Philadelphia chromosome results in the enzyme tyrosine kinase being produced in the bone marrow, and it is this enzyme that causes too many of the myeloid stem cells to take the path of converting into granulocytes, rather than red blood cells or platelets. CML can occur at any age however it most often appears in adults with a median age of 60-65 years. There are three phases of the disease that consist of an initial (indolent) chronic phase, lasting a median of 3 years, which typically transforms into an accelerated phase, followed by a blast phase or "blast crisis," which is usually the terminal event. Conventional-dose regimens used for chronic-phase disease can induce multiple remissions and delay the onset of blast crisis to a median of 4–6 years. However, successive remissions are invariably shorter and more difficult to achieve than their predecessors.

Imatinib mesylate (Gleevec®), a selective inhibitor of the abnormal BCR-ABL TK protein, is considered the treatment of choice for newly diagnosed CML. While imatinib can be highly effective in suppressing CML in most patients, it is not curative and is ineffective in 20% to 30%, initially or due to development of BCR-ABL mutations that cause resistance to the drug. Dasatinib and nilotinib, two other TK inhibitors (TKIs), have received marketing approval from the U.S. Food and Drug Administration (FDA) to treat CML following failure or patient intolerance of imatinib. However, allogeneic hematopoietic stem-cell transplantation (HSCT) remains the only treatment capable of inducing durable remissions or cure in CML patients.

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). HSCs are created in the bone marrow and are found in the bone marrow and peripheral blood. There is also a high concentration of HSCs in umbilical-cord blood. HSCT can be either autologous (using the person’s own stem cells) or allogeneic (using stem cells from a donor). In allogeneic HSCT, it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed based on variability at three of more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). As HLA variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease (GVHD), also increase.

Donor lymphocyte infusion (DLI) is a form of adoptive immunotherapy and may be requested to induce a graft versus leukemia, or graft versus tumor, response without requiring the recipient to undergo additional high-dose chemotherapy. Donor lymphocytes are collected from the original donor through leukapheresis. The collection of donor lymphocytes is an outpatient procedure for the donor. Lymphocytes are then either infused via vein into the recipient or are frozen for a more clinically appropriate time.

The goal of the pretransplant evaluation is to assess the ability of a patient to tolerate the surgery, post-operative

immunosuppression, and transplant care. An extensive cardiopulmonary evaluation, screening for occult infection or cancer, and psychosocial evaluation is standard. Specific testing varies depending upon the patient's age, medical history, and transplant center practice. In addition, while a certain battery of tests may initiate the work up, more testing may be indicated depending upon the condition of the patient or the initial test results. In addition to a standard medical evaluation the initial assessment should include a psychological and social support evaluation to identify issues that may impair a successful outcome after transplantation. These include a lack of information about the nature of the transplant procedure and post-transplant care, drug or alcohol dependence, compliance with complex medical and behavior regimens. The assessment includes education of the family and the support network of the patient because compliance with complex medical and behavior treatment is critical after any organ transplant procedure. Recipients must be able to incorporate complicated medications, follow-up appointments, and frequent laboratory visits into their schedules. Having an adequate support network aware of these requirements will encourage patient compliance and long-term success.

COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be reviewed by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, State regulations, and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Office visits with participating Providers do NOT require prior authorization. Providers should see the Member in office visits as soon as possible and without delay. Failure to see the Member in office visits may be considered a serious quality of care concern.

Transplant Evaluation

(Chao 2022; NCCN 2022; Deeg & Sandmaier 2022; NCI 2022; Negrin 2021; Negrin 2020; Schiffer & Atallah 2020; CMS 2016; ECOG date unknown; [1-5] NMDP date unknown)

Please see *MCP-323 Pre-Transplant Evaluation* for additional criteria and information.

Components of the transplant evaluation include:

1. History and physical examination; **AND**
2. Psychosocial evaluation and clearance:
   a. No behavioral health disorder by history or psychosocial issues:
      - If history of behavioral health disorder, no severe psychosis or personality disorder;
      - Mood/anxiety disorder must be excluded or treated;
      - Member has understanding of surgical risk and post procedure compliance and follow-up required.

   AND
   b. Adequate family and social support.

AND

3. EKG; **AND**
4. Chest x-ray; **AND**
5. Cardiac clearance in the presence of any of the following:
   a. Chronic smokers; **OR**
   b. Members > 50 years age; **OR**
   c. Those with a clinical or family history of heart disease or diabetes.

AND

6. Pulmonary clearance if evidence of pulmonary artery hypertension or chronic pulmonary disease; **AND**

7. Neurological exam and clearance for transplant including **ONE** of the following:
    a. Normal neurologic exam; **OR**
    b. Non-life limiting neurological impairment that does not preclude transplant and not caused by hematologic malignancy (e.g., diabetic peripheral neuropathy); **OR**
    c. Abnormal neurological exam with positive findings including **ONE** of the following:
        - Lumbar puncture normal cytology; **OR**
        - Lumbar puncture with cytological exam abnormal, however central nervous system disease treated prior to clearance.

AND

8. A Performance Status that includes **ONE** of the following:
    a. Karnofsky score 70-100%; **OR**
    b. Eastern Cooperative Oncology Group (ECOG) Grade 0-2.

AND

9. Lab studies that include:
    a. Complete blood count; kidney profile (blood urea nitrogen, creatinine); electrolytes; calcium; phosphorous; albumin; liver function tests; and coagulation profile (prothrombin time, and partial thromboplastin time);*
    b. Serologic screening for: Human Immunodeficiency Virus (HIV); Epstein Barr virus (EBV); Hepatitis B virus (HBV); Hepatitis C virus (HCV); cytomegalovirus (CMV); rapid plasma reagin (RPR) and/or fluorescent treponemal antibody (FTA):*
        - If HIV positive **ALL** of the following must be met:
            i. CD4 count >200 cells/mm-3 for >6 months; **AND**
            ii. Human Immunodeficiency Virus 1 (HIV-1) ribonucleic acid undetectable; **AND**
            iii. On stable anti-retroviral therapy >3 months; **AND**
            iv. No other complications from Acquired Immunodeficiency Syndrome (AIDS) (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm).
    c. Urine drug screen if Member is current or gives a history of past drug abuse.

AND

10. Colonoscopy (if indicated or if Member is age ≥ 45) with complete workup and treatment of abnormal results as indicated; an initial screening colonoscopy after initial negative screening requires a follow-up colonoscopy every 10 years).*

AND

11. Gynecological examination with Pap smear for women ages ≥ 21 to ≤ 65 years of age or if indicated (not indicated in women who have had a total abdominal hysterectomy or a total vaginal hysterectomy) within the last three years with complete workup and treatment of abnormal results as indicated.*

Within the last 12 months:

1. Dental examination or oral exam showing good dentition and oral care or no abnormality on panorex or plan for treatment of problems pre- or post-transplant; **AND**
2. Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated;* **AND**
3. Prostate Specific Antigen (PSA) if history of prostate cancer or previously elevated PSA with complete workup and treatment of abnormal results as indicated.*

* Participating Centers of Excellence may waive these criteria.

Criteria for Allogeneic HSCT

(Chao 2022; NCCN 2022; Deeg & Sandmaier 2022; NCI 2022; Negrin 2021; Negrin 2020; Schiffer & Atallah 2020; CMS 2016; ECOG date unknown; [1-5] NMDP date unknown)

Allogeneic HSCT *ablative or non-myeloablative* from a HLA-matched donor (e.g., at least six out of eight match of the HLA-A, HLA-B, HLA-C and HLA-DRB1 markers) or from cord blood when there are no matched sibling or unrelated donors (e.g. at least four out of six match of the HLA-A, HLA-B and HLA-DRB-1 markers) **may be authorized** in adults and children for the treatment of CML when **ALL** of the following criteria are met:

1. All transplant criteria are met; **AND**

2. The requesting transplant recipient should not have any of the following **absolute contraindications**:
   a. Cardiac, pulmonary, and nervous system disease that cannot be corrected and is a prohibitive risk for surgery; **OR**
   b. Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer); **OR**
   c. Systemic and/or uncontrolled infection; **OR**
   d. AIDS (CD4 count < 200cells/mm3); **OR**
   e. Unwilling or unable to follow post-transplant regimen as evidenced by **ONE** of the following:
      - Documented history of non-compliance; **OR**
      - Inability to follow through with medication adherence or office follow-up.

   OR
   f. Chronic illness with one year or less life expectancy; **OR**
   g. Limited, irreversible rehabilitation potential; **OR**
   h. Active untreated substance abuse issues (requires documentation supporting that Member is free from addiction for minimally 6 months if previous addiction was present); **OR**
   i. No adequate social or family support.

AND

3. The requesting transplant recipient should be evaluated carefully and potentially treated if any of the relative contraindications below are present. (Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation).
   a. Smoking, documentation supporting free from smoking for 6 months; **OR**
   b. Active peptic ulcer disease; **OR**
   c. Active gastroesophageal reflux disease; **OR**
   d. Cerebrovascular accident (CVA) with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months; **OR**
   e. Obesity with body mass index of >30 kg/m^2 may increase surgical risk; **OR**
   f. Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hepatologist; **OR**
   g. Gall bladder disease requires ultrasound of the gall bladder with treatment prior to transplantation.

In addition, coverage is indicated for adults who are ≥ age 18 with **ANY** of the following clinical indications:

1. Hematologic / Cytogenetic Response
   a. No hematologic response* after 3 months of oral TKI (imatinib, dasatinib, nilotinib) therapy; **OR**
   b. No cytogenetic response.^

   * Complete hematologic response (CHR) is defined by a white blood cell count <10,000/microL with no immature granulocytes and <5 percent basophils on differential; platelet count <450,000/microL; and spleen not palpable.

   ^ Cytogenetic response is classified according to the percent Philadelphia chromosome positive cells into none (>95 percent), minimal (66 to 95 percent), minor (36 to 65 percent), major (1 to 35 percent), and complete (no Philadelphia chromosome positive cells). For patients with an inadequate number of metaphases, complete cytogenetic response can also be documented by FISH of blood interphase cell nuclei demonstrating <1 percent BCR-ABL1-positive nuclei of at least 200 nuclei.

OR

2. Those in cytogenetic relapse at 6, 12, or 18 months, after achieving initial hematologic remission after 3 months of imatinib therapy; **OR**

3. Progressing on an oral TKI to accelerated phase, defined by **one or more** of the following:
   a. 10 to 19 percent blasts in the peripheral blood or bone marrow; **AND/OR**
   b. Peripheral blood basophils ≥20 percent; **AND/OR**
   c. Platelets <100,000/microL, unrelated to therapy; **AND/OR**
   d. Platelets >1,000,000/microL, unresponsive to therapy; **AND/OR**
   e. Progressive splenomegaly and increasing white cell count, unresponsive to therapy; **AND/OR**
   f. Cytogenetic evolution (defined as the development of chromosomal abnormalities in addition to the Philadelphia chromosome).

OR

4. Progressing on a TKI to Blast crisis (myeloid or lymphoid), defined by **ANY** of the following:
   a. ≥20 percent peripheral blood or bone marrow blasts; **OR**
   b. Large foci or clusters of blasts on the bone marrow biopsy; **OR**
   c. Presence of extramedullary blastic infiltrates (e.g., myeloid sarcoma, also known as granulocytic sarcoma or chloroma).

OR

5. Intolerance to TKI.

Criteria for Subsequent HSCT

A second or repeat allogeneic HSCT (ablative or non-myeloablative) **may be authorized** only one time for Members with CML who meet **ALL** of the following criteria:

1. Member meets the above criteria for transplant; **AND**
2. Primary graft failure indicated by no signs of engraftment* by 42 days after the transplant; **OR**
3. Failure to engraft.*

*Engraftment is defined as the first 3 consecutive days on which the absolute neutrophil count (ANC) exceeds 0.5 x 10^9/L or > ANC500 at any time after transplantation.

Criteria for DLI

DLI collection and cryopreservation **may be authorized** following a medically necessary allogeneic HSCT (NCCN 2022; Chao 2022):

1. For incomplete chimerism and disease relapse in the setting of incomplete chimerism (defined as incomplete donor stem cell grafting in the recipient's bone marrow); **AND**
2. Donor lymphocytes must be collected from the original hematopoietic stem cell donor.

Continuation of Therapy

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

1. If Molina Healthcare has authorized prior requests for transplantation **ALL** of the following information is required for medical review:
   a. Presence of no absolute contraindication as listed above; **AND**
   b. History and physical within the last 12 months; **AND**
   c. Kidney profile within the last 12 months; **AND**
   d. Cardiac update if history of cardiac disease within two years (≥ 50 years of age); **AND**
   e. Psychosocial evaluation or update within the last 12 months; **AND**

f. Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

2. If authorized prior requests for transplantation were obtained from another insurer, **ALL** of the following information is required for medical review:
   a. Authorization letter/documentation from previous insurer; **AND**
   b. Presence of no absolute contraindication as listed above; **AND**
   c. History and physical within the last 12 months; **AND**
   d. Cardiac update if history of cardiac disease within two years (≥ 50 years of age); **AND**
   e. Psychosocial evaluation or update within the last 12 months; **AND**
   f. Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

For Members with Significant or Daily Cannabis Use

1. Documentation of compliance with a physician prescribed and managed program of abstinence, and a reasonable expectation that the Member will be abstinent from cannabis use during the transplant and immediate post-transplant time period. Daily cannabis use is an absolute contraindication for both transplant and pre-transplant evaluation unless there is a state mandate applicable for medical cannabis use and transplants, and there is documentation of Member compliance with a physician prescribed plan of care for prescribed cannabis use.
2. If the Member's cannabis use follows a formal, State-based program for managed medical cannabis, the request should include:
   - Documentation of the Plan of Care for medical cannabis (including the medical decision making that supports the use of medical cannabis); **AND**
   - Transplant Provider agreement with the Plan of Care (including agreement to be accountable for managing the Member's use of medical cannabis).

Limitations and Exclusions

The items below **are not considered medically necessary.** This list includes, but is not limited to:

1. Allogeneic (ablative or non-myeloablative) HSCT when the above criteria are not met.
2. Patients with refractory progressive disease occurring more than 12 months after the discontinuation of treatment.
3. Autologous HSCT in individuals with CLL or SLL.
4. HSC collection, storage and freezing for a future unplanned transplant is not covered.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The published, peer-reviewed scientific literature supports the safety and effectiveness of allogeneic HSCT for the treatment of CML in selected individuals. However, improved outcomes have not been demonstrated for autologous HSCT compared with conventional chemotherapy in individuals with CML therefore the role of autologous HSCT for this indication has not been established. A summary of the most relevant medical evidence is outlined below.

Masouridi-Levrat et al. (2022) completed a prospective study that included 383 patients to determine if prior treatment with a second-generation TKI (2GTKI) before allogenic HSCT influenced engraftment and non-relapse mortality (NRM) rates. Secondary outcomes measured included rates of acute and chronic GVHD and hepatic sinusoidal obstruction

syndrome (SOS). Patients were placed into groups that received dasatinib (n=155), nilotinib (n=64), or sequential treatment of dasatinib and nilotinib with or without bosutinib and/or ponatinib (n=164). Most patients (n=306) had imbatinib as the primary TKI. Median follow-up time after allogeneic HSCT was 37 months. The disease status at the start of the 2GTKI was reported for 265 patients: 123 were in chronic phase 1 (CP1), 67 were in advanced phase (AP) or > CP1, and 75 were in blast crisis (BC). The overall disease status at the time of allogeneic HSCT was reported for 361 patients: 139 were in CP1, 163 in AP or > CP1, and 59 were in BC. Engraftment was able to be evaluated in 379 patients with 350 achieving engraftment, 10 experiencing primary graft failure, and 19 experiencing secondary graft failure. Overall NRM was 18% at 12-months and 24% at 5-years following allogeneic HSCT. Acute GVHD was evaluable in 347 patients with approximately 34% of patients experiencing grade II-IV acute GVHD at a median time of 0.9 months. Chronic GVHD was evaluable in 314 patients with an incidence rate of 60% by the 5-year mark. Median time to chronic GVHD was 5.7 months. Disease relapse occurred in 29% of patients at 2-years and 36% at 5-years. Overall survival (OS) at 2-years was 65.4% and 56% at 5-years. SOS occurred in 6 cases with most of those cases occurring in the dasatinib group (n=5). The SOS rate was 2% in this study which is much lower than previously reported rates of 25% in other studies. Researchers noted an advanced disease stage at the start of 2GTKI and allogeneic HSCT had a negative impact on OS and relapse-free survival rates. OS rates at 5-years were 67% for CP1, 57% for AP or > CP1, and 37% for BC. Researchers reported that allogeneic HSCT could be considered prior to a third line TKI therapy in CP1 due to transplantation rates appear better with pre-transplantation 2GTKI treatment.

Yassine et al. (2022) performed a systematic review and meta-analysis to determine the efficacy of allogeneic HSCT in patients with TKI-resistant chronic phase CML (CP-CML). The meta-analysis included 9 studies with a total of 439 patients. Patients were stratified based on age groups determined by the researchers. Patients were placed in the pediatric group if they were < 18 years of age. Patients ≥ 18 years of age were placed into the adult group. Some of the studies included in the meta-analysis either did not group patients according to age or used overlapping age groups. Patients in those studies were placed into a separate “mixed/unclear population” group. The primary goals of the study were participant characteristics, clinical outcomes based on benefits, progression-free survival (PFS), disease-free survival (DFS), complete remission (CR), molecular response (MR), NRM, relapse, acute GVHD, and chronic GVHD. Stratification of the included studies resulted in 3 studies (n=200 patients) for the adult group, 1 study (n=28 patients) for the pediatric group, and 5 studies (n=211) for the mixed/unclear population group. The pooled outcomes based on benefits for adults was 84%, pediatrics was 91%, and the mixed/unclear population was 76%. PFS was only reported in studies stratified into the mixed/unclear population group. The pooled PFS rates for the mixed/unclear population was 82%. The pooled DFS rates for adults and the mixed/unclear population was 66% and 47% respectively. CR was only reported in 1 study stratified to the adult population and was 56%. The pooled MR rates for adults and the mixed/unclear population was 88% and 89% respectively. The pooled NRM rates for adults and the mixed/unclear population was 20% and 28% respectively. The pooled relapse rates for adults and the mixed/unclear population were 19% and 27% respectively. Acute and chronic GVHD rates were only reported in studies stratified to the mixed/unclear population and were 46% and 51% respectively. Limitations of the study included the inability of researchers to compare outcomes to regimen intensity and outcomes could not be analyzed separately for patients with TKI resistance versus TKI intolerance.

Hu et al. (2020) completed a meta-analysis to estimate and compare residual life expectancy (RLE) for patients diagnosed with CP-CML based on the timing of allogeneic HSCT versus continuation of TKI therapy. Researchers noted the effective timing of allogeneic HSCT in CP-CML has not been determined due to TKI therapy being considered the first-line treatment for CML due to high-efficacy, tolerable side effects, and the availability of multiple TKIs that make it easier to switch TKIs. Data was pooled from 2 large databases: the Center for International Blood and Marrow Transplantation Research and the MD Anderson Cancer Center. The Center for International Blood and Marrow Transplantation Research database provides detailed data on autologous and allogeneic HSCT. The MD Anderson Cancer Center database provides detailed data on patients treated with TKI therapy. Researchers included patients in the meta-analysis if they were between the ages of 18 and 65 years and if they had been diagnosed with Philadelphia chromosome or BCR-ABL1-positive CP-CML. Patients in the MD Anderson Cancer Center database were excluded if they had previously received either autologous or allogeneic HSCT, had switched TKIs for any reason other than failure, and had remained on their initial TKI. A total of 1361 patients were included in the meta-analysis with 138 of those patients being in the TKI cohort and 1223 in the allogeneic HSCT cohort. Median follow-up time was 96.4 months for the TKI cohort and 59.6 months for the allogeneic HSCT cohort. Researchers noted that most transplanted patients received myeloablative allogeneic HSCT (n=1029). Researchers found that allogeneic HSCT was associated with worse OS compared to a change to a second TKI. There was also increased mortality in matched unrelated donor transplants versus matched related donor transplants. The mean RLE was 7.1 years for patients undergoing allogeneic

HSCT in CP1 CML versus 8.5 years if they did not receive allogeneic HSCT. CP1 CML patients already on a second TKI had improved outcomes if they switched to a third TKI (mean RLE 8.5 years) versus receiving allogeneic HSCT (mean RLE 6.8 years). Chronic phase 2 patients had a mean RLE of 4.7 years if they received allogeneic HSCT versus 7.4 years if they continued with TKI therapy. Patients with accelerated phase CML had a similar RLE between allogeneic HSCT (mean 5.3 years) and continuation of TKI therapy (mean 5.6 years). Blast phase CML patients showed notable improvement in RLE with allogeneic HSCT (mean 2.6 years) versus continuation of TKI therapy (mean 1.5 years).

National and Specialty Organizations

The **National Cancer Institute (NCI)** guidelines for allogeneic HSCT in CML recommend considering allogeneic HSCT early in the chronic phase in patients younger than 60 years of age with an identical twin or with HLA-matched siblings despite the procedure being associated with considerable morbidity and mortality. The NCI also recommends allogeneic HSCT as the preferred choice of treatment for patients that are intolerant of or have a poor response to TKI therapy, certain patients that have a T315I mutation, and certain patients in the blastic phase. Progressively worse outcomes have been noted when using allogeneic HSCT in the accelerated and blast phases (NCI 2023).

The **National Comprehensive Cancer Network (NCCN)** (2023) guidelines for CML recommend consideration of allogeneic bone marrow transplant for treatment of CML for individuals with high-disease risk score upon diagnosis. Since response rates with TKIs have been favorable as an initial treatment option (first- and second-line therapies) for CP-CML, HSCT is no longer recommended as a first-line treatment option for CP-CML. Recommendations for allogeneic HSCT include:

- Those who have BP-CML at diagnosis;
- Those who have an inadequate, no response or progress while on TKIs;
- Those who have AP-CML, BP-CML, T315I and other BCR-ABL1 mutations and are unresponsive or intolerant to all TKIs;
- Those who have progression of CML to accelerated or blast phase on TKI therapy;
- Survival rates are better for individuals transplanted in chronic phase versus those with advanced disease.
- Five-year survival for individuals with chronic, accelerated and blast crisis phases treated with matched-related transplants are approximately 75%, 40% and 10% respectively.

The **American Society for Transplantation and Cellular Therapy (ASTCT)** guidelines recommend allogeneic HSCT in early CP-CML. Autologous HSCT is not recommended in clinical practice for any stage of CML based on available evidence (Kanate et al. 2020).

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

Code	Description
	Collection Codes
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
	Cell Processing Services
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
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
	Cell infusion codes
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38242	Allogeneic lymphocyte infusions
38243	Hematopoietic progenitor cell (HPC); HPC boost
	Histocompatibility Codes
86812	HLA typing; A, B, or C (e.g., A10, B7, B27), single antigen
86813	HLA typing; A, B, or C, multiple antigens
86816	HLA typing; DR/DQ, single antigen
86817	HLA typing; DR/DQ, multiple antigens

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	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 of pre-and post-transplant care in the global definition

APPROVAL HISTORY

04/10/2024 Correction to ANC value in coverage section. Annual review scheduled for June 2024.
06/14/2023 Policy reviewed with the following changes to criteria: "Pre-Transplant Evaluation" changed to "Transplant Evaluation," new criteria 7b, removal of abnormal serology criteria from 9b, criteria 10 changed to age 45 years, asterisk added to criteria 11 to denote it may be waived by a Center of Excellence, and acronyms used for consistency with remainder of policy. Overview, Summary of Medical Evidence, and References sections updated. "Marijuana" replaced with "cannabis" throughout policy. Added codes 86812, 86813, 86816, 86817 and updated code descriptions for 38240, 38241, 38242, and 38243. ICD-10 codes removed. Supplemental Information section removed. Grammatical edits to Disclaimer section and Documentation Requirements. Policy reviewed on May 17, 2023, by a practicing, board-certified physician in the areas of Medical Oncology and Hematology.
06/08/2022 Policy reviewed, no changes to criteria; included section on marijuana use; updated references.
06/09/2021 Policy reviewed; updated guidelines and references.
06/17/2020 Policy reviewed; updated guidelines and references.
06/19/2019 Policy reviewed; updated guidelines and references.
06/10/2018 Policy reviewed; updated guidelines and references.
07/27/2017 Updated Summary of Medical Evidence section and references.
06/15/2016 Policy reviewed, no changes.
12/16/2015 Policy reviewed, no changes.
06/02/2015 Updated pre-transplant criteria, continuation of therapy, absolute and relative contraindications, and coding sections.
07/25/2014 New policy.

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