Hematopoietic Stem-Cell Transplantation for Chronic Myelogenous Leukemia

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Original Effective Date: 04/01/2008  
Line(s) of Business: HMO; PPO  
Current Effective Date: 01/23/2015  
Section: Transplants  
Place(s) of Service: Outpatient; Inpatient  

Precertification is required for this service.

I. Description

Hematopoietic Stem-Cell Transplantation

Hematopoietic stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naïve” and thus are associated with a lower incidence of rejection or graft-versus-host disease (GVHD).

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HSCT. However, immunologic compatibility between donor and patient is a critical factor for achieving a good outcome of allogeneic HSCT. Compatibility is established by typing of human leukocyte antigens (HLAs) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the HLA A, B, and DR loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci.

Conventional Preparative Conditioning for HSCT

The conventional (“classical”) practice of allogeneic HSCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total-body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is due to a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect that develops after engraftment of allogeneic stem cells within the patient’s bone marrow space. While the slower GVM effect is considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of
Hematopoietic Stem Cell Transplantation for Chronic Myelogenous Leukemia

pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include pre-engraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allogeneic HSCT, immune suppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility of the patient to opportunistic infections. The immune reactivity between donor T cells and malignant cells that is responsible for the GVM effect also leads to acute and chronic GVHD.

The success of autologous HSCT 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 prior to undergoing bone marrow ablation. As a consequence, autologous HSCT is typically performed as consolidation therapy when the patient’s disease is in complete remission. Patients who undergo autologous HSCT are susceptible to chemotherapy-related toxicities and opportunistic infections prior to engraftment, but not GVHD.

Reduced-Intensity Conditioning for Allogeneic HSCT

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and non-relapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative, to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allogeneic HSCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For the purposes of this Policy, the term “reduced-intensity conditioning” will refer to all conditioning regimens intended to be non-myeloablative, as opposed to fully myeloablative (conventional) regimens.

For CML, RIC regimens were initially used to extend the use of allogeneic HSCT to the estimated 70% of CML patients who were ineligible for myeloablative conditioning regimens because of advanced age or comorbidities. The use of RIC and allogeneic HSCT is of particular interest for treatment of CML given the relatively pronounced susceptibility of this malignancy to the graft versus leukemia (GVL) effect of allogeneic hematopoietic progenitor cells following their engraftment in the host.
Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a hematopoietic stem-cell disorder that is characterized by the presence of a chromosomal abnormality called the Philadelphia chromosome, which results from reciprocal translocation between the long arms of chromosomes 9 and 22. This cytogenetic change results in constitutive activation of BCR-ABL, a tyrosine kinase (TK) that stimulates unregulated cell proliferation, inhibition of apoptosis, genetic instability, and perturbation of the interactions between CML cells and the bone marrow stroma only in malignant cells. CML accounts for about 15% of newly diagnosed cases of leukemia in adults and occurs in about 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 that are secondary to anemia and splenomegaly. CML is diagnosed 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.

Therapy for Chronic Myelogenous Leukemia

Historically, the only curative therapy for CML in blast phase was HSCT, and HSCT 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-alpha.

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. Even so, the overall survival (OS) of patients who present in chronic phase is greater than 95% at 2 years and 80% to 90% at 5 years.

Two other TK inhibitors (TKIs; dasatinib, nilotinib) have received marketing approval from the U.S. Food and Drug Administration to treat CML as front-line therapy or following failure or patient intolerance of imatinib. Two additional TKIs, bosutinib and ponatinib, have been approved for use for patients resistant or intolerant to prior therapy.

For patients who progress on imatinib, the therapeutic options include increasing the imatinib dose, changing to another TKI, or allo-HSCT. Detection of BCR-ABL mutations may be important in determining an alternative TKI; the presence of T315I mutation is associated with resistance to all TKIs and should indicate the need for allo-HSCT or an experimental therapy.
TKIs have been associated with long-term remissions; however, if progression occurs on TKI therapy, allo-HSCT is generally indicated and offers the potential for cure. In any case, allogeneic HSCT remains the only treatment capable of inducing durable remissions or cure in CML patients.

II. Criteria/Guidelines
A. Allogeneic hematopoietic stem-cell transplantation (HSCT) using a myeloablative conditioning regimen is covered as a treatment of chronic myelogenous leukemia.

B. Allogeneic hematopoietic stem-cell transplantation using a reduced-intensity conditioning regimen is covered as a treatment of chronic myelogenous leukemia in patients who meet clinical criteria for an allogeneic HSCT but who are not considered candidates for a myeloablative conditioning allogeneic HSCT.

III. Policy Guidelines
A. Some patients for whom a conventional myeloablative allotransplant could be curative may be considered candidates for reduced-intensity conditioning (RIC) allogeneic hematopoietic stem-cell transplantation (HSCT). These include those patients whose age (typically older than 60 years) or comorbidities (eg, liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning regimen.

B. For patients who qualify for a myeloablative allogeneic HSCT on the basis of clinical status, either a myeloablative or reduced-intensity conditioning regimen may be covered.

IV. Limitations/Exclusions
Autologous stem-cell transplantation as a treatment of chronic myelogenous leukemia is not covered as it is not known to be effective in improving health outcomes.

V. Administrative Guidelines
A. Precertification is required for a transplant evaluation and for the transplant itself and should be submitted by the proposed treating facility. To precertify, please complete HMSA’s Precertification Request and mail or fax the form as indicated along with the required documentation.

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### Hematopoietic Stem-Cell Transplantation for Chronic Myelogenous Leukemia

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<td>Cord blood-derived stem-cell transplantation, allogeneic</td>
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ICD-10 codes are provided for your information. These will not become effective until 10/01/2015

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VI. Scientific Background

This policy has been updated regularly with searches of the MEDLINE database. The most recent literature search was performed through November 3, 2014. Following is the summary of the key literature to date.

Allogeneic Hematopoietic Stem-Cell Transplantation

Allogeneic hematopoietic stem-cell transplantation (HSCT) is the only known potentially curative therapy for chronic myelogenous leukemia (CML). It became a standard of treatment for CML in the 1980s when the graft-versus-leukemia (GVL) effect was shown to be the critical factor for long-term disease control.(1) Studies in patients with chronic phase disease who received an human leukocyte antigen (HLA)—matched sibling donor transplant had a 45% to 75% probability of long-term disease-free survival, while those transplanted with more advanced disease had a 15% to 40% long-term survival.(2) Young, good-risk patients transplanted early in the chronic phase from HLA-matched but unrelated donors had a 40% to 60% probability of long-term survival, although it is lower than that of similar patients transplanted from matched sibling donors.

CML was once the most common malignancy for which allogeneic HSCT was performed, but by 2005, it was in eighth place among hematologic transplantation indications. A retrospective analysis of data from the Center for International Blood and Marrow Transplant Research Center showed that transplantation for CML was in decline prior to U.S. Food and Drug Administration approval of imatinib in 2001. Subsequently, long-term follow-up results from the International Randomized Study of Interferon and STI 571 (IRIS) of imatinib mesylate, plus the availability of 2 additional approved TKI agents (nilotinib and dasatinib), have caused modification of the timing of application of allogeneic HSCT. This procedure now is typically delayed in patients with newly diagnosed CML, who will receive imatinib mesylate a TKI agent as front-line treatment. Allogeneic HSCT may be used early in the disease course when a complete molecular response to the drug fails or is not achieved soon after starting TKI therapy, or after relapse.

HSCT with Nonmyeloablative Conditioning

Techniques for allogeneic HSCT have continued to develop, with important advancements in the use of nonmyeloablative or reduced-intensity conditioning (RIC) preparative regimens. Overall, among 9 studies compiled in a recent review, outcomes achieved with RIC allogeneic transplants have been similar to those with conventional allotransplants, with overall survival (OS) rates ranging from 35% at 2.5 years to 85% at 5 years among patients in chronic phase 1 at transplant. Among the studies included in this review, treatment-related mortality or nonrelapse mortality ranged from 0% to 29% at 1 year. In the largest experience, a retrospective European Group for Blood and Marrow Transplantation study of 186 patients, OS was 54% at 3 years using a variety of RIC regimens in patients in chronic phase 1 (n=118), chronic phase 2 (n=26), acute phase (n=30),
and blast crisis (n=12). Among patients transplanted in the first chronic phase OS was 69% at 3 years.

RIC regimens have many of the same limitations as standard-intensity conditioning: relapse, graft-versus-host disease (GVHD) (particularly chronic GVHD), and mortality from treatment-related causes other than myelotoxicity. However, in the absence of prospective, comparative, randomized trials, only indirect comparisons can be made between the relative clinical benefits and harms associated with myeloablative and RIC regimens with allogeneic HSCT. Comparison of study results is further compromised by heterogeneity among patients, treatments, and outcome measures. Nonetheless, clinical evidence suggests outcomes in CML are similar with myeloablative and RIC allogeneic HSCT. Thus, RIC allogeneic HSCT should be considered medically necessary for CML patients who would otherwise be expected to benefit from an allogeneic HSCT.

**HSCT in the Context of TKI Therapy for CML**

The advent of tyrosine kinase inhibitor (TKI) therapy has altered the treatment paradigm for CML such that the majority of patients are treated initially with a TKI until disease progresses. While progression may occur within months of starting a TKI, this may be delayed for years, as shown by the results of the IRIS trial and other studies. With the addition of 3 other TKIs (nilotinib, dasatinib and bosutinib) plus the possibility of effective dose escalation with imatinib to override resistance, it is possible to maintain a typical CML patient past the upper age limit (usually 50-55 years) at which a myeloablative allogeneic HSCT is considered an option. These patients would be eligible for a RIC allogeneic HSCT.

The optimal timing for HSCT in the context of TKI therapy is still being evaluated. Liu et al evaluated outcomes for chronic-phase CML patients who underwent HSCT after imatinib failure. The authors retrospectively evaluated 105 patients with newly-diagnosed chronic-phase CML seen at a single institution from 1999 to 2011. Sixty-six patients received first-line imatinib therapy, 26 (treated before 2003) received interferon followed by imatinib, and 13 received front-line allo-HSCT with curative intent. Twenty-two (21.0%) patients received allo-HSCT overall, including 13 as front-line therapy and 9 following imatinib failure. Compared with those who received front-line allo-HSCT, those who underwent HSCT following imatinib failure had higher European Group for Blood and Bone Marrow Transplantation (EBMT) risk score (p=0.03). Among patients receiving allo-HSCT (n=22), patients with imatinib failure and disease progression had a significantly worse OS (p=0.015) compared with those receiving allo-HSCT as front-line therapy (median follow-up, 134 months, range, 6-167 months). One patient died of relapse and 1 of chronic GVHD among patients receiving front-line allo-HSCT, with a 3-year survival rate of 91.7% (95% confidence interval [CI], 29 to 38 months).

Zhao et al reported outcomes for 12 patients with CML with disease progression on imatinib who were treated with either dasatinib or nilotinib followed by allo-HSCT at a single center. Four patients died: 1 of primary disease and 3 of transplant-related complications. After a median follow-up of 28 months (range, 12-37 months) after HSCT, 8/12 (66.7%) patients were alive, including 7 with complete molecular remission.
Lee et al attempted to identify predictors of outcomes in patients who underwent allogeneic HSCT for CML in chronic phase. Ninety-seven patients were included, 47 of whom were TKI-naive and 50 of whom had received 1 or more TKI therapy before HSCT. Most (N=48) of the TKI-recipient had received imatinib as initial therapy; 2 had received second-generation TKIs (dasatinib, bosutinib). After a median follow-up of 115.8 months, 4-year OS and event-free survival were 80.4% and 58.8%, respectively. Multivariate analysis showed that there were no differences in survival outcomes based on prior TKI therapy. However, in multivariate models, age at transplant was significantly associated with relapse and transplant-related mortality, while graft source (peripheral blood vs bone marrow) was significantly associated with event-free survival. The authors conclude that their findings confirm prior researchers’ findings that pretreatment with imatinib does not affect survival outcomes after allogeneic HSCT for CML.

In addition to being used before HSCT, TKI therapy may be used after HSCT to prevent or treat disease relapse. Egan et al conducted a retrospective analysis of patients at a single institution who underwent allogeneic HSCT for CML and Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) at a single institution with detectable BCR-ABL transcripts and RNA available for sequencing of the ABL kinase domain in both the pre- and post-HSCT settings to evaluate the impact of pre-HSCT mutations in the ABL kinase domain on post-HSCT relapse. Among 95 patients with CML with available polymerase chain reaction transcripts, 10 (10.5%) were found to have pre-HSCT ABL kinase mutations known to confer resistance to TKIs. Of those with CML, 88.4% underwent myeloablative chemotherapy and 11.6% underwent nonmyeloablative chemotherapy. Twenty-nine CML patients received post-HSCT TKIs, 19 (65.5%) for prophylaxis and 10 (34.5%) for treatment of refractory or relapsed disease. In 9 (64.2%) of the 14 patients with pre-HSCT mutations (both CML and Philadelphia chromosome-positive ALL), the same mutation conferring TKI resistance was also detectable after HSCT. Among the 14 with pre-HSCT mutations, 8 (57.1%) received a TKI in the post-HSCT setting, and 7 (50%) demonstrated post-HSCT refractory disease or relapse. Of the 7 with relapsed disease, 5 had been given a predictably ineffective TKI based on mutation status in the first 100 days after HSCT.

Section Summary:
Allogeneic HSCT is accepted as a standard treatment in CML, although the use of targeted TKI therapy has allowed many patients who would previously have required HSCT to forestall or avoid HSCT. Evidence suggests that HSCT following nonmyeloablative conditioning regimens has similar outcomes to HSCT after myeloablative conditioning regimens. Although research into the optimal timing of HSCT in the setting of TKI therapy is limited, the available evidence suggests that pre-treatment with TKIs does not worsen outcomes after HSCT.

**Autologous HSCT**
A major limitation in the use of autologous HSCT in patients with CML is a high probability that leukemic cells will be infused back into the patient. However, it is recognized that many CML patients still have normal marrow stem cells. Techniques used to isolate and expand this normal clone of cells have included ex vivo purging, long-term culture, and immunophenotype selection. Even without such techniques, there have been isolated case reports of partial cytogenetic...
remissions after autologous HSCT, and 1 study has suggested that patients undergoing such therapy may have improved survival compared with historical controls.

Another article summarized the results of 200 consecutive autologous transplants using purged or unpurged marrow from 8 different transplant centers. Of the 200 patients studied, 125 were alive at a median follow-up of 42 months. Of the 142 transplanted in chronic phase, the median survival had not been reached at the time of publication, while the median survival was 35.9 months for those transplanted during an accelerated phase. Other data consist of small, single institution case series using a variety of techniques to enrich the population of normal stem cells among the harvested cells. Additional reports of small, uncontrolled studies with a total of 182 patients (range, 15–41 patients) given autotransplants for CML included patient populations that varied across the studies. Some focused on newly diagnosed patients or those in the first year since diagnosis. Others focused on patients who did not respond to or relapsed after initial treatment using interferon alfa. Finally, some focused on patients transplanted in the late chronic phase or after transformation to accelerated phase or blast crisis. Although some patients achieved complete or partial molecular remissions and long-term disease-free survival, these studies do not permit conclusions free from the influence of patient selection bias. All autotransplanted patients included in these reports were treated before imatinib mesylate or newer TKIs became available. Since these agents have been shown to induce major hematologic and, less often, cytogenetic remissions, even among patients in accelerated phase and blast crisis, future studies of autotransplants for CML may focus on patients who fail or become resistant to imatinib mesylate. Alternatively, it may be incorporated into combination regimens used for high-dose therapy.

**Ongoing Clinical Trials**

A search of online database ClinicalTrials.gov in November 2014 identified a number of phase 2 and 3 trials evaluating HSCT for CML, many of which are evaluating various conditioning regimens, stem-cell sources, and mobilization protocols. The following are phase 3 trials of HSCT for CML currently underway:

- **Graft-Versus-Host Disease Prophylaxis in Treating Patients With Hematologic Malignancies Undergoing Unrelated Donor Peripheral Blood Stem-Cell Transplant (NCT01231412)** – This is a randomized, open-label trial to evaluate the use of total body irradiation together with fludarabine phosphate, cyclosporine, mycophenolate mofetil, or sirolimus before donor peripheral blood stem-cell transplant in the prevention of GVHD for patients with a variety of hematologic malignancies. The primary outcome is the rate of acute grade II to IV GVHD, exclusive of GVHD that occurs as a result of alterations to immunosuppressive therapy in response to relapse or progression. Enrollment is planned for 300 subjects; the estimated study completion date is September 2015.

- **Imatinib Mesylate With or Without Interferon Alfa or Cytarabine Compared With Interferon Alfa Followed by Donor Stem-Cell Transplant in Treating Patients With Newly Diagnosed Chronic Phase Chronic Myelogenous Leukemia (NCT00055874)** – This is a randomized Phase 3 trial to compare imatinib mesylate with or without interferon alfa or cytarabine with interferon
alfa followed by donor stem-cell transplant for patients with newly diagnosed CML. Primary outcome measures are OS, risk group-dependent survival, progression-free survival, and hematologic, cytogenetic, and molecular response rates. Enrollment is planned for 1600 subjects; the estimated study completion date is December 2016.

- A Phase III Study of Fludarabine and Busulfan Versus Fludarabine, Busulfan and Low-Dose Total Body Irradiation in Patients Receiving an Allogeneic Hematopoietic Stem-Cell Transplant (NCT01366612) – This is a randomized, open-label trial to compare the addition of total body irradiation with standard pre-transplant conditioning in patients undergoing allogeneic HSCT for a variety of hematologic malignancies, including CML. Enrollment is planned for 54 subjects; the estimated study completion date is December 2014.

Summary of Evidence

Allogeneic hematopoietic stem-cell transplant (HSCT) has been accepted as a standard treatment in chronic myelogenous leukemia. However, introduction of the tyrosine kinase inhibitors (TKIs) imatinib, dasatinib, nilotinib, bosutinib, and ponatinib has significantly changed the practice of HSCT for CML. TKIs have replaced HSCT as initial therapy in patients with chronic phase CML. However a significant proportion of cases fails to respond to TKIs, develop resistance to them, or become unable to tolerate all TKIs and go on to allogeneic HSCT. In addition, allogeneic HSCT represents the only potentially curative option for those patients in accelerated or blast phase. The currently-available evidence suggests that TKI-pretreatment does not lead to worse outcomes if HSCT is needed. Allogeneic HSCT using a myeloablative conditioning regimen may be considered medically necessary as a treatment of CML. In addition, allogeneic HSCT using a reduced-intensity conditioning (RIC) regimen may be considered medically necessary as a treatment of CML in patients who meet clinical criteria for an allogeneic HSCT but who are not considered candidates for a myeloablative conditioning allogeneic HSCT.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN) Guidelines

The 2015 NCCN guidelines (v1.2015) recommend allogeneic bone marrow transplant as an alternative treatment option only for high-risk settings. The use of first-line treatment with allogeneic HSCT for:

- Patients presenting with blast phase at diagnosis.
- Patients with T315I and other BCR-ABL1 mutations that are resistant to all TKIs.
- Rare patients intolerant to all TKIs.

For chronic phase CML:

- Allogeneic HSCT is recommended for patients with T315I mutations that are resistant to all TKIs.
- Evaluation for HSCT is recommended if the response milestones are not achieved, as indicated by:
Hematopoietic Stem-Cell Transplantation for Chronic Myelogenous Leukemia

- BCR-ABL1/ABL1 >10% or lack of partial cytogenetic response (PCyR) at 3 and 6 months.
- Minor or no cytogenetic response at 12 months.
- Less than complete cytogenetic response (CCyR) at 18 months.
- Cytogenetic relapse at 12 or 18 months.

- For advanced phase CML, allogeneic HSCT should be considered for patients with AP-CML or BP-CML.

Autologous bone marrow transplant for CML is not addressed in the NCCN guidelines.

European LeukemiaNet Guidelines

In 2013, European LeukemiaNet issued updated guidelines for the management of CML. These guidelines recommend the use of allogeneic HSCT in the following situations:

- For chronic phase treatment:
  - Consider HSCT as second-line therapy after failure of nilotinib or dasatinib as first-line therapy.
  - Recommend HSCT in all eligible patients as third-line therapy after failure of or intolerance to 2 TKIs.
  - Consider HSCT at any point if T315I mutation.

- For accelerated or blast phase in newly-diagnosed, TKI-naive patients:
  - Begin imatinib or dasatinib.
  - Recommend HSCT for all blast phase patients and for accelerated phase patients who do not achieve an optimal response.

- For accelerated or blast phase as progression from chronic phase in TKI-pretreated patients: recommend HSCT for all patients (after initiation of one of the TKIs that was not previously used or ponatinib in the case of T315I mutations).

VII. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not
be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VIII. References


29. Blue Cross Blue Shield Assocation. Hematopoietic Stem-Cell Transplantation for chronic Myelogenous Leukemia. 8.01.30; Updated December 2014.