



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Stem-Cell Transplantation for Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML)**

**Effective Date ..... 11/15/2010**  
**Next Review Date.....11/15/2011**  
**Coverage Policy Number ..... 0243**

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## Hyperlink to Related Coverage Policies

Donor Leukocyte Infusions  
Stem-Cell Transplantation for Myelodysplastic Syndrome  
Transplant Donor Charges  
Umbilical Cord Blood Banking

## INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

## Coverage Policy

**CIGNA covers allogeneic hematopoietic stem-cell transplantation (HSCT) as medically necessary for the treatment of chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML) when a human leukocyte antigen (HLA) matched donor (at least five of six match) is available.**

**CIGNA does not cover autologous HSCT for the treatment of CMML or JMML because it is considered experimental, investigational or unproven.**

## General Background

Chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML) are clonal disorders characterized by both dysplastic and proliferative features. They are classified by the World Health Organization as myelodysplastic/myeloproliferative neoplasms (MDS/MPD) (National Cancer Institute [NCI], 2010).

Median age for individuals with chronic myelomonocytic leukemia (CMML) is 65 to 70 years, with 75% over age 60. Median survival for CMML ranges from 12–24 months, with a progression to acute leukemia in 15%–20% of cases (National Cancer Institute [NCI], 2010). Poor prognosis is associated with low hemoglobin level, low platelet count with high white blood cell, monocyte and lymphocyte counts, the presence of circulating, immature

myeloid cells, a high percentage of marrow blasts, a low percentage of marrow erythroid cells, abnormal cytogenetics, and high levels of serum lactate dehydrogenase (LDH) and beta2-microglobulin (Onida, 2002)

Median age for JMML is 1.8 years. Prognosis is poor and the disorder is resistant to standard dose chemotherapy. The median survival is 10 months to four years; prognosis is related to the age at diagnosis (NCI, 2010). Children less than one year at diagnosis have a better prognosis than children at other ages.

For both CMML and juvenile myelomonocytic leukemia (JMML) various standard-dose chemotherapy regimens have been used with only modest success; responses achieved are usually of short duration (NCI, 2010). Approximately 10% to 20% of children will progress to a blast-like phase consistent with acute myelogenous leukemia (Smith, 2008). Bone marrow transplantation or hematopoietic stem-cell transplantation (HSCT) seem to offer the best chance of cure (NCI, 2010; Smith, 2008).

### **Stem-Cell Transplantation**

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) 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). HSCT can be either autologous (i.e., using the patient's own stem cells), or allogeneic (i.e., using stem cells from a donor).

**Allogeneic HSCT:** Hematopoietic stem-cell transplantation (HSCT) is an acceptable treatment option for selected individuals with CMML and JMML. "Bone marrow transplantation or HSCT appears to be the only current treatment that alters the natural history of CMML" (NCI, 2010). Allogeneic HSCT is generally considered in younger, healthy patients with appropriate donor matches. Age and performance status are critical factors that may influence ability to tolerate intensive therapies.

Although disease relapse, treatment-related mortality (TRM) and graft-versus-host disease (GVHD) remain issues associated with allogeneic HSCT for CMML, this treatment option offers the best chance for cure. Several retrospective studies have demonstrated improved overall survival (OS) with myeloablative allogeneic HSCT with estimated OS rates of 10%–41% at two- to five years (Elliot, 2006; Karrabul, 2005; Kroger, 2002; Arnold, 1998).

Allogeneic HSCT also offers the best chance of cure for JMML (NCI, 2010; Smith, 2008; Hasle, 2007). Several retrospective reviews have demonstrated three- and five-year OS of 50% and 32%–64%, respectively (Yoshima, 2007; Locatelli, 2005). In a review of outcomes of 183 patients registered in the prospective and retrospective studies of the European Working Group on Myelodysplastic Syndrome in Childhood involving second allogeneic transplantation of 24 children with JMML, Yoshima (2007) noted an event-free survival of 52% at five years, however, relapse rates were 33%–40%, five-year cumulative incidence of mortality was 27%.

Although data are not robust, non-myeloablative chemotherapy with allogeneic HSCT is also an accepted treatment option for individuals with CMML and JMML. Outcomes are similar to those seen with myelodysplastic syndromes (MDS) as these disorders share dysplastic characteristics. Laporte et al. (2008) reported outcomes of 148 individuals with myelodysplastic syndromes and myeloproliferative disorders, including seven with CMML, who underwent allogeneic HSCT with nonmyeloablative conditioning. Three-year relapse-free and overall survival rates in the individuals with CMML were 43% and 43%, respectively.

**Autologous HSCT:** Data are lacking regarding outcomes with autologous HSCT for the treatment of CMML and JMML. The role of this therapy has not been established for this indication.

### **Contraindications**

Many factors affect the outcome of a tissue transplant; the selection process is designed to obtain the best result for each individual. The presence of any significant comorbid conditions which would significantly compromise clinical care and chances of survival is a contraindication to transplant. Advanced age in the setting of myeloablative chemotherapy may limit survival; greater age is associated with a higher incidence of post-transplantation complications. Relative contraindications to HSCT include, but are not limited to:

- poor cardiac function (ejection fraction less than 45%)
- poor liver function (bilirubin greater than 2.0 mg/dL and transaminases greater than two times normal), unless related to acute myelogenous leukemia

- poor renal function (creatinine clearance less than 50 mL/min)
- poor pulmonary function (diffusion capacity less than 60% of predicted)
- presence of human immunodeficiency virus or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1)
- Karnofsky rating less than 60% and/or Eastern Cooperative Oncology Group (ECOG) performance status greater than 2

**Professional Societies/Organizations**

**Lymphoma and Leukemia Society:** Notes “Allogeneic stem cell transplantation is the only known curative option for JMML patients. This treatment has been noted to achieve long-term survival in up to 50% of patients but relapses are known to occur in up to 30% to 40% of patients after transplantation. Second transplants have been beneficial for some patients.” “Allogeneic stem cell transplantation has been used to treat and sometimes cure CMML patients.”

**National Cancer Institute (NCI):** The NCI (2010) notes “Bone marrow/stem-cell transplantation appears to be the only current treatment that alters the natural history of chronic myelomonocytic leukemia (CMML). Regarding juvenile myelomonocytic leukemia (JMML) the NCI (2010) notes that “No consistently effective therapy is available for JMML.” “Bone marrow transplantation seems to offer the best chance for a cure.”

**National Comprehensive Cancer Network™ (NCCN™):** NCCN (2010) Practice Guidelines note “Allogeneic HSCT from an HLA-matched sibling donor is a preferred approach for treating a portion of patients with MDS. Standard conditioning is used for relatively younger patients, while the approach using nonmyeloablative conditioning is preferable in older individuals.”

**Summary**

The published, peer-reviewed scientific literature supports the safety and effectiveness of allogeneic hematopoietic stem-cell transplantation (HSCT) for selected individuals with chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML). Data are lacking regarding the safety and effectiveness of autologous HSCT for CMML and JMML. The role of autologous HSCT for the treatment of CMML and JMML has not been established.

**Coding/Billing Information**

**Note:** This list of codes may not be all-inclusive.

**Covered when medically necessary:**

CPT®* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-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
38230	Bone marrow harvesting for transplantation

38240	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions

HCCPS Codes	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic
S2150 <sup>†</sup>	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

<sup>†</sup> **Note:** Covered when medically necessary and when used to report allogeneic bone-marrow or blood-derived stem cell procedures.

ICD-9-CM Diagnosis Codes	Description
205.10	Chronic myeloid leukemia without mention of remission
205.11	Chronic myeloid leukemia in remission

#### Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous

\*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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## Policy History

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<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	11/15/2008	0243	Stem-Cell Transplant for Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML)

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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA's subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.