



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)

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

INSTRUCTIONS FOR USE

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Coverage Policy

CIGNA covers myeloablative 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 covers non-myeloablative allogeneic HSCT as medically necessary for the treatment of CMML and JMML when the individual is not a candidate for myeloablative allogeneic HSCT and an 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 Diseases (MDS/MPD) (National Cancer Institute [NCI], 2008). Median age for individuals with CMML is 65 to 70 years, with 75% over age 60; median age for JMML is one year.

Median survival for CMML ranges from 12–24 months, with a progression to acute leukemia in 15%–20% of cases (NCI, 2008). 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)

JMML also has a poor prognosis and is resistant to standard dose chemotherapy. The median survival is 10 months to four years; prognosis is related to the age at diagnosis (NCI, 2008). Children < one year at diagnosis have a better prognosis than children at other ages.

Various chemotherapy regimens have been used with only modest success in CMML and JMML. Responses achieved are usually of short duration (NCI, 2008). Allogeneic hematopoietic stem-cell transplantation has been used with some success in the treatment of other myelodysplastic and myeloproliferative disorders and is an accepted therapy for the treatment of CMML and JMML in selected individuals.

Stem-Cell Transplant

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). HSC transplantation (HSCT) can be either autologous (i.e., using the patient's own stem cells) or allogeneic (i.e., using stem cells from a donor).

Myeloablative Allogeneic HSCT: HSCT is the only therapy that alters the natural history of CMML and offers a chance for cure (NCI, 2008). The individual's International Prognostic Scoring System risk category is used in planning treatment options, which may include allogeneic HSCT. Myeloablative allogeneic stem-cell transplantation 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 and graft-versus-host disease remain issues associated with myeloablative allogeneic HSCT for CMML, this treatment option offers the best chance for cure for this disease. Several retrospective studies have demonstrated improved overall survival with myeloablative allogeneic HSCT with estimated overall survival rates of 10%–41% at two- to five years (Elliot, 2006; Karrabul, 2005; Kroger, 2002; Arnold, 1998).

HSCT also offers the best chance of cure for JMML (NCI, 2008; Hasle, 2007; Niemeyer, 1997). Several retrospective reviews have demonstrated three- and five-year survival rates 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%.

Non-Myeloablative Allogeneic HSCT: Non-myeloablative allogeneic HSCT is a feasible option for patients with MDS for whom fully ablative dose chemotherapy followed by allogeneic HSCT is not appropriate; likewise, this therapy may result in improved outcomes for patients with CMML and JMML, as these disorders share dysplastic characteristics.

Studies regarding the use of non-myeloablative preparative regimens followed by allogeneic HSCT have included recipients with various hematological conditions classified as MDS, including JMML and CMML. Several prospective case series have demonstrated the efficacy of this therapy in patients with high-risk MDS who are over age 50 (Laporte, 2008; Aloysius, 2004; de Lima, 2004; Taussig, 2003; Chakraverty, 2002; Martino, 2002). Event-free survival rates ranged from 43%–73%, although time intervals assessed were varied. The treatment resulted in low rates of severe graft-versus-host disease and treatment-related mortality.

Autologous Transplant: There is a paucity of data regarding autologous HSCT for the treatment of chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML). Overall, there is insufficient evidence in the published peer-reviewed medical literature to support the use of autologous hematopoietic stem-

cell transplantation (HSCT) for the treatment of chronic myelomonocytic leukemia (CMML) or juvenile myelomonocytic leukemia (JMML).

Contraindications

Many factors affect the outcome of a tissue transplant; the selection process is designed to obtain the best result for each individual. Overall health, age and disease stage are extremely important considerations in evaluating transplant candidates. 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

National Cancer Institute (NCI): The NCI (2008) notes bone marrow/stem cell transplantation appears to be the only current treatment that alters the natural history of CMML. Regarding JMML the NCI (2008) 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): The NCCN (2009) Practice Guidelines in Oncology for Myelodysplastic Syndromes note that 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

There is sufficient evidence in the published, peer-reviewed scientific literature to support the use of myeloablative allogeneic hematopoietic stem-cell transplantation for the treatment of chronic myelomonocytic leukemia (CMML) and juvenile myelomonocytic leukemia (JMML). Non-myeloablative allogeneic HSCT is an accepted treatment option for selected individuals with 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

HCPCS Codes	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

[†]**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®) © 2008 American Medical Association: Chicago, IL.

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Policy History

<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.