

Clinical Policy: Nonmyeloablative Allogeneic Stem Cell Transplants

Reference Number: CP.MP.141

Last Review Date: 02/20

[Coding Implications](#)

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Allogeneic hematopoietic stem cell transplants that do not destroy all of the hematopoietic cells in the bone marrow are termed reduced-intensity or nonmyeloablative conditioning regimens. Although there are no clear definitions, reduced-intensity conditioning (RIC) generally destroys more hematopoietic cells and is more toxic than nonmyeloablative conditioning, but less so than myeloablative conditioning. Both nonmyeloablative and RIC regimens are categorized as non-fully ablative regimens, and are used interchangeably in this policy, unless otherwise noted. RIC/nonmyeloablative approaches can circumvent the need for high-dose conditioning regimens that are associated with organ toxicity and mortality, while maintaining adequate response in certain cancers and blood disorders.

Note: Please refer to CP.MP. 108 for requests for Allogeneic Hematopoietic Cell Transplants for Sickle Cell Anemia and β -Thalassemia

Please refer to CP.MP. 162 Tandem Transplant if request is for an allogeneic reduced conditioning transplant for multiple myeloma in a tandem transplant.

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation[®] that nonmyeloablative/RIC allogeneic transplants are **medically necessary** for members who meet all of the following criteria:
 - A. Candidate for allogeneic stem cell transplantation for any of the following diagnoses:
 1. Acute lymphoblastic leukemia;
 2. Acute myelogenous leukemia;
 3. Aplastic anemia;
 4. Paroxysmal nocturnal hemoglobinuria;
 5. Chronic lymphocytic leukemias;
 6. Chronic myelogenous leukemia;
 7. Congenital immunodeficiency syndromes: molecular remissions induced by Gleevec
 8. Hodgkin's lymphoma (formerly Hodgkin's disease): primary refractory or relapsed, including those who have relapsed having an autologous bone marrow transplant
 9. Non-Hodgkin's lymphoma, any of the following:
 - a. Primary refractory or relapsed, including those who have relapsed after having an autologous bone marrow transplant (excluding diffuse large B-cell lymphoma);
 - b. Follicular lymphomas;
 - c. Mantle cell lymphoma;
 - d. Diffuse large B-cell lymphoma that is in remission following second-line therapy for relapsed or refractory disease;
 10. Myelodysplastic syndromes;
 11. Myelofibrosis.

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- B. Unsuitable for conventional high-dose myeloablative allografting because of untreatable significant dysfunction of another major organ system and/or severe comorbidities, including, but not limited to, any of the following:
 1. Bilirubin > 2 mg/dL;
 2. Hemostasis: international normalized ratio (INR) > 1.6 (unless on oral anticoagulants);
 3. Cardiac function: multigated acquisition scan (MUGA) or echocardiogram with ejection fraction (EF) < 45%;
 4. Pulmonary function:
 - a. Forced expiratory volume in 1 second (FEV1) ≤ 50% of predicted value; or
 - b. Diffusing capacity of the lung for carbon monoxide (DLCO) ≤ 50% of predicted value;
 5. Performance scale index:
 - a. Karnofsky or Lansky score < 70%; or
 - b. Eastern Cooperative Oncology Group (ECOG) performance score ≤ 2;
- C. Does not have ANY of the following absolute contraindications:
 1. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
 2. Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy that are perceived to increase the risk of non-adherence after transplantation;
 3. Psychiatric or psychological condition associated with the inability to cooperate or comply with medical therapy;
 4. Absence of an adequate or reliable social support system;
 5. Substance abuse or dependence (including tobacco and alcohol) without convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence. Serial blood and urine testing may be used to verify abstinence from substances that are of concern.

II. It is the policy of health plans affiliated with Centene Corporation that nonmyeloablative/RIC allogeneic transplants are **experimental / investigational** for the following indications:

- A. Astrocytomas and gliomas
- B. Beta thalassemia
- C. Breast cancer
- D. Dermatomyositis
- E. Ewing sarcoma
- F. Germ cell Tumors
- G. Idiopathic thrombocytopenic purpura
- H. Juvenile rheumatoid arthritis
- I. Lupus erythematosus
- J. Medulloblastoma
- K. Melanoma
- L. Multiple sclerosis
- M. Osteosarcoma
- N. Ovarian epithelia and mixed epithelia/germ cell cancers
- O. Polycythemia vera

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- P. Polymyositis
- Q. Ovarian germ cell Tumors
- R. Primitive Neuroectodermal Tumors (PNET), including medulloblastoma and ependymoma
- S. Renal cell carcinoma
- T. Retinoblastoma
- U. Rhabdomyosarcoma
- V. Severe systemic rheumatoid arthritis, adult and juvenile
- W. Sarcoma
- X. Systemic lupus erythematosus
- Y. Systemic sclerosis
- Z. Testicular Cancer
- AA. Wilms tumor
- BB. Multiple myeloma (except in tandem transplant- refer to CP.MP. 162)
- CC. Neuroblastoma.

Background

Allogeneic stem cell transplant (AlloBMT) has been used as a treatment for cancer and diseases of the blood system for many years. For this treatment, stem cells are collected from either related or unrelated donors. During the conditioning phase, high doses of chemotherapy (HDC), with or without radiation therapy, are used to eradicate the disease and this is followed by infusion of an allogeneic stem cell transplantation to rescue bone marrow and restore normal immune function. Major limitations of this technique are the associations with serious side effects and high mortality. All stem cell transplants (SCTs) preparative regimens have the potential for extensive toxicity. Loss of appetite and energy, alopecia, and nausea/vomiting are very frequent and add to poor physical and emotional tolerance of the transplant procedure. In addition, mucositis, diarrhea, and transient pancytopenia are inevitable side effects of most preparative regimens, and these complications are synergistic in dramatically increasing the risk of bacterial and fungal infections. Any decrease in toxicity, without concomitant loss of efficacy, would be desirable.

Myeloablative means that the treatment kills (ablates) the myeloid stem cells in the bone marrow, the cells that produce new blood cells. Several less intense conditioning regimens have been developed recently and rely more on immuno-suppression than cytotoxic effects to permit engraftment of donor cells. These regimens are collectively termed nonmyeloablative. Studies have shown that donor allogeneic stem cells can engraft in recipients using less-intensive conditioning regimens that are sufficiently immunosuppressive to permit graft-host tolerance. This manifests as a stable mixed donor-host hematopoietic chimerism, a term which means coexistence of donor and recipient cells. Once chimerism has developed, a further infusion of donor leukocytes may be given to eradicate malignant cells by inducing a graft vs. tumor effect. Nonmyeloablative allogeneic transplants, also referred to as “mini-transplant” or “transplant lite”, are thought to be potentially as effective as conventional HDC followed by an allogeneic stem cell transplantation, but with decreased morbidity and mortality related to the less intense nonmyeloablative chemotherapy conditioning regimen. Consequently, for patients with malignancies that are eligible for conventional HDC/AlloBMT, conditioning with milder, nonmyeloablative regimens represents a variation of an established procedure.

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Coding Implications

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| CPT® Codes | Description |
|-------------------|--|
| 38204 | Management of recipient hematopoietic progenitor cell donor search and cell acquisition |
| 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, 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 deletion within harvest. T-cell depletion |
| 38211 | Transplant preparation of hematopoietic progenitor cells; tumor 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; allogeneic |
| 38240 | Hematopoietic progenitor cell (HPC), allogeneic transplantation per donor |

| HCPCS Codes | Description |
|--------------------|--|
| S2142 | Cord blood-derived stem cell transplantation, allogeneic |
| S2150 | Bone marrow or blood-derived peripheral 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 |

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

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| ICD 10 CM Code | Description |
|----------------|--|
| C74.00-C74.92 | Malignant neoplasm of adrenal gland |
| C81.00-C96.9 | Malignant neoplasm of lymphoid, hematopoietic and related tissue |
| D46.0-D46.9 | Myeloplastic syndromes |
| D56.0-D56.9 | Thalassemia |
| D57.00-D57.819 | Sickle-cell disorders |
| D59.5 | Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli] |
| D61.01-D61.09 | Constitutional aplastic anemia |
| D75.81 | Myelofibrosis |
| Z51.11 | Encounter for antineoplastic chemotherapy |
| Z94.84 | Stem cells transplant status |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|--|-------|---------------|
| Policy adopted from HN version | 03/17 | 4/17 |
| Clarified in I. that policy statements applied to RIC and nonmyeloablative regimens. Removed criteria in I.A. that patient be a candidate for conventional allogeneic transplantation. Added paroxysmal nocturnal hemoglobinuria as an indication. Changed chronic lymphoblastic leukemia to chronic lymphocytic leukemia. Added criteria to multiple myeloma requiring that it be responsive to primary treatment. For myelodysplastic syndromes, restricted indication to adults. Added myelofibrosis as an indication. Edited comorbidity in criteria I.B. to include the listed comorbidities as well as others not mentioned – “including but not limited to.” Removed contraindication in II.A. of ineligibility for conventional high-dose chemotherapy/myeloablation, as well as restriction for members under 3 years of age. | 02/18 | 02/18 |
| Updated description. Moved beta thalassemia and sickle cell anemia from the list of approved indications to the list of E/I indications. Removed age restriction from myelodysplastic syndromes. Added to the multiple myeloma indication that an RIC/NMA approach is appropriate post – autologous or fully myeloablative stem cell transplant. Removed diffuse large b-cell lymphoma from E/I list. Clarified that diffuse large cell lymphoma is diffuse large b-cell lymphoma, and added requirement that the patient is in remission following second-line therapy for relapsed or refractory disease. Specialist reviewed. | 02/19 | 02/19 |
| Added note to refer to CP.MP.108 for requests for Allogeneic HCT’s for Sickle Cell Anemia and β-Thalassemia and CP.MP.162 if request is for a tandem transplant for multiple myeloma. Clarified in I.A.8. that Hodgkin’s disease is now referred to as Hodgkin’s lymphoma. Moved multiple myeloma and neuroblastoma from list of approved indications to the list of E/I indications. Removed sickle cell anemia from list of E/I indications. Removed CPT 38206 as code is for autologous transplant. Added ICD-10 Codes: D59.5, D75.81 | 02/20 | 02/20 |

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

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for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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