



Clinical Policy: Hematopoietic Stem-Cell Transplantation For Multiple Myeloma and Primary Amyloidosis

Reference Number: WNC.CP.243

Last Review Date: 11/2023

[Coding Implications](#)

[Revision Log](#)

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

Note: 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.

Description¹

This policy describes the medical necessity criteria for Hematopoietic Stem-Cell Transplantation (HSCT) For Multiple Myeloma and Primary Amyloidosis.

Policy/Criteria¹

- I. WellCare of North Carolina[®] shall cover HSCT for **Multiple Myeloma (MM)** in **ANY** of the following situations:
 - A. A single or second (salvage) autologous HSCT to treat MM;
 - B. Tandem autologous-autologous hematopoietic stem-cell transplantation to treat multiple myeloma in beneficiaries who fail to achieve at least a near complete or very good partial response after the first transplant in tandem sequence.
 - C. Tandem transplantation with an initial round of autologous hematopoietic stem-cell transplantation followed by a non-marrow-ablative conditioning regimen and allogeneic hematopoietic stem-cell transplantation (i.e., reduced-intensity conditioning transplant) to treat newly diagnosed MM.

- II. WellCare of North Carolina[®] shall cover HSCT for **POEMS syndrome and Primary Amyloidosis** in the following situations:
 - A. Autologous stem cell transplantation to treat disseminated POEMS syndrome;
 - B. Autologous stem cell transplantation to treat primary systemic amyloidosis.

- III. WellCare of North Carolina[®] **shall not** cover HSCT for Multiple Myeloma, POEMS Syndrome and Primary Amyloidosis in the following situations:
 - A. When the criteria listed in Section I are not met;
 - B. Allogeneic HSCT, myeloablative or nonmyeloablative, as upfront therapy of newly diagnosed multiple myeloma or as salvage therapy;
 - C. Allogeneic and tandem HSCT to treat POEMS syndrome and primary systemic amyloidosis;
 - D. When the beneficiary's psychosocial history limits the beneficiary's ability to comply with pre- and post-transplant medical care; **or**
 - E. Current beneficiary or caretaker non-compliance would make compliance with a disciplined medical regimen improbable.

CLINICAL POLICY WNC.CP.243**HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS****Background¹**

Hematopoietic stem-cell transplantation refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiation therapy. 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 human leukocyte antigens (HLA) 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.

Multiple myeloma is a systemic malignancy of plasma cells that represents approximately 10% of all hematologic cancers. It is treatable but rarely curable, with estimated new cases and deaths in 2010 in the United States 20,180 and 10,650, respectively. At the time of diagnosis most patients have generalized disease, and, the selection of treatment is influenced by patient age, general health, prior therapy, and the presence of complications of the disease.

The disease is staged by estimating tumor mass, based on various clinical parameters like hemoglobin, serum calcium, number of lytic bone lesions, and the presence or absence of renal failure. Multiple myeloma usually evolves from an asymptomatic premalignant stage (termed “monoclonal gammopathy of undetermined significance” or MGUS). Treatment is usually reserved for patients with symptomatic disease (usually progressive myeloma), whereas asymptomatic patients are observed, as there is little evidence that early treatment of asymptomatic multiple myeloma prolongs survival when compared to therapy delivered at the time of symptoms or end organ damage. In some patients, an intermediate asymptomatic but more advanced premalignant stage is recognized and referred to as smoldering multiple myeloma. The overall risk of disease progression from smoldering to symptomatic multiple myeloma is 10% per year for the first 5 years, approximately 3% per year for the next 5 years, and 1% for the next 10 years.

The **primary amyloidosis** comprise a group of diseases with an underlying clonal plasma cell dyscrasia. They are characterized by the extracellular deposition of pathologic, insoluble protein fibrils with a beta-pleated sheet configuration that exhibit a pathognomonic red-green birefringence when stained with Congo red dye and examined under polarized light. These diseases are classified on the basis of the type of amyloidogenic protein involved, as well as by the distribution of amyloid deposits. In systemic amyloidosis, the unnatural protein is produced at a site that is remote from the site(s) of deposition, whereas in localized disease the protein is

CLINICAL POLICY WNC.CP.243

HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS

produced at the site of deposition. Light-chain amyloidosis (AL), the most common type of systemic amyloidosis, has an incidence similar to that of Hodgkin’s lymphoma or chronic myelogenous leukemia, estimated at 5 to 12 people per million annually. The median age at diagnosis is around 60 years. The amyloidogenic protein in AL amyloidosis is an immunoglobulin (Ig) light chain or light-chain fragment that is produced by a clonal population of plasma cells in the bone marrow. While the plasma cell burden in AL amyloidosis is typically low, ranging from 5%–10%, this disease also may occur in association with multiple myeloma in 10%–15% of patients. Deposition of AL amyloidogenic proteins causes organ dysfunction, most frequently in the kidneys, heart, and liver, although the central nervous system and brain may be affected.

Historically, this disease has had a poor prognosis, with a median survival from diagnosis of about 12 months, although outcomes have improved with the advent of combination chemotherapy with alkylating agents and autologous HSCT. Emerging approaches include the use of immunomodulating drugs such as thalidomide or lenalidomide, and the proteasome inhibitor bortezomib. Regardless of the approach chosen, treatment of AL amyloidosis is aimed at rapidly reducing the production of amyloidogenic monoclonal light chains by suppressing the underlying plasma cell dyscrasia, with supportive care to decrease symptoms and maintain organ function. The therapeutic index of any chemotherapy regimen is a key consideration in the context of underlying organ dysfunction.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2023, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Reviews, Revisions, and Approvals	Reviewed Date	Approval Date
Original approval date	04/21	05/21
Reviewed CPT codes.	12/21	02/22
Annual Review	11/22	11/22
NCHC verbiage removed from NC Guidance Verbiage.	04/23	04/23
Annual Review. CPT codes removed.	11/23	11/23

References

1. State of North Carolina Medicaid. Medicaid and Health Choice Clinical Coverage Policy No: 11A-8 Hematopoietic Stem-Cell Transplantation For Multiple Myeloma and Primary Amyloidosis. [Program Specific Clinical Coverage Policies | NC Medicaid \(ncdhhs.gov\)](https://www.ncdhhs.gov/program-specific-clinical-coverage-policies) Published July 1, 2021. Accessed August 8, 2023.

CLINICAL POLICY WNC.CP.243

HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS

North Carolina Guidance

Eligibility Requirements

- a. An eligible beneficiary shall be enrolled in the NC Medicaid Program (Medicaid is NC Medicaid program, unless context clearly indicates otherwise);
- b. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.
- c. The Medicaid beneficiary may have service restrictions due to their eligibility category that would make them ineligible for this service.

EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age

- a. 42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]
Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiary under 21 years of age if the service is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed practitioner).

This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his or her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product or procedure:

1. that is unsafe, ineffective, or experimental or investigational.
2. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

CLINICAL POLICY WNC.CP.243

HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS

EPSDT and Prior Approval Requirements

1. If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does NOT eliminate the requirement for prior approval.
2. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *NCTracks Provider Claims and Billing Assistance Guide*, and on the EPSDT provider page. The Web addresses are specified below:

NCTracks Provider Claims and Billing Assistance Guide:

<https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html>

EPSDT provider page: <https://medicaid.ncdhhs.gov/>

Provider(s) Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for the procedure, product, or service related to this policy, the provider(s) shall:

- a. meet Medicaid qualifications for participation;
- b. have a current and signed Department of Health and Human Services (DHHS) Provider Administrative Participation Agreement; and
- c. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

Compliance

Provider(s) shall comply with the following in effect at the time the service is rendered:

- a. All applicable agreements, federal, state and local laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements; and
- b. All NC Medicaid's clinical (medical) coverage policies, guidelines, policies, provider manuals, implementation updates, and bulletins published by the Centers for Medicare and Medicaid Services (CMS), DHHS, DHHS division(s) or fiscal contractor(s).

Claims-Related Information

Provider(s) shall comply with the NC Tracks Provider Claims and Billing Assistance Guide, Medicaid bulletins, fee schedules, NC Medicaid's clinical coverage policies and any other relevant documents for specific coverage and reimbursement for Medicaid:

- a. Claim Type - as applicable to the service provided:
Professional (CMS-1500/837P transaction)
Institutional (UB-04/837I transaction)
Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.
- b. International Classification of Diseases and Related Health Problems, Tenth Revisions, Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS) - Provider(s) shall report the ICD-10-CM and Procedural Coding System (PCS) to the highest level of specificity that supports medical necessity. Provider(s) shall use the current ICD-10 edition and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for code description, as it is no longer documented in the policy.

CLINICAL POLICY WNC.CP.243

HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS

- c. Code(s) - Provider(s) shall report the most specific billing code that accurately and completely describes the procedure, product or service provided. Provider(s) shall use the Current Procedural Terminology (CPT), Health Care Procedure Coding System (HCPCS), and UB-04 Data Specifications Manual (for a complete listing of valid revenue codes) and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for the code description, as it is no longer documented in the policy. If no such specific CPT or HCPCS code exists, then the provider(s) shall report the procedure, product or service using the appropriate unlisted procedure or service code.

Unlisted Procedure or Service

CPT: The provider(s) shall refer to and comply with the Instructions for Use of the CPT Codebook, Unlisted Procedure or Service, and Special Report as documented in the current CPT in effect at the time of service.

HCPCS: The provider(s) shall refer to and comply with the Instructions For Use of HCPCS National Level II codes, Unlisted Procedure or Service and Special Report as documented in the current HCPCS edition in effect at the time of service

- d. Modifiers - Providers shall follow applicable modifier guidelines.
- e. Billing Units - Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).
- f. Co-payments -
For Medicaid refer to Medicaid State Plan:
<https://medicaid.ncdhhs.gov/get-involved/nc-health-choice-state-plan>
- g. Reimbursement - Provider(s) shall bill their usual and customary charges. For a schedule of rates, refer to: <https://medicaid.ncdhhs.gov/>.

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

CLINICAL POLICY WNC.CP.243**HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR MULTIPLE MYELOMA AND PRIMARY AMYLOIDOSIS**

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

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.