Clinical Policy: Allogeneic Hematopoietic Cell Transplant for β-Thalassemia

Reference Number: KY.CP.MP.108
Date of Last Revision: 11/25

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

This policy describes the medical necessity requirements for allogeneic hematopoietic cell transplants for β–thalassemia. β–thalassemia is a hemoglobinopathy caused by deleterious genetic alterations in hemoglobin. This monogenic disease presents a range of heterogeneous symptoms that stem from damaged red blood cell function.[1] Despite its limitations, allogeneic hematopoietic cell transplant is the only curative therapy possible for this hemoglobinopathy.

Note: *For criteria related to Zynteglo, please see CP.PHAR.545 Betibeglogene Autotemcel (Zynteglo).*

Policy/Criteria

I. It is the policy of WellCare of Kentucky that allogeneic hematopoietic cell transplants for homozygous β-thalassemia are **medically necessary** when all the following criteria are met:

A. HLA-matched donor is available, one of the following:
   1. Cord blood is the source of stem cells;
   2. Bone marrow is the source of stem cells;
   3. Peripheral blood is the source, and the donor is either unable to, or refuses to donate bone marrow;
   4. Transfusion-dependent due to thalassemia;
   5. A standard, myeloablative conditioning regimen will be used;

B. Does not have ANY of the following absolute contraindications:
   1. Infections with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
   2. Inability to adhere to the regimen necessary to preserve the transplant, even with caregiver support;
   3. Active substance use or dependence including current tobacco use, vaping, marijuana use (unless prescribed by a licensed practitioner), or IV drug use without convincing evidence of risk reduction behaviors (unless urgent transplant timelines are present, in which case a commitment to reducing behaviors is acceptable).

Note: Data suggests that younger recipients have better outcomes following AHCT than those who are older at the time of transplant.

II. It is the policy of WellCare of Kentucky that there is insufficient evidence regarding the safety and efficacy of the following:

A. Autologous hematopoietic cell transplant for β-thalassemia not in the context of gene therapy;
B. Allogeneic hematopoietic cell transplants for the treatment of homozygous *β*-Thalassemia for any-indications other than those specified above.

Background

Hemoglobinopathies are a group of over 1,000 hematological disorders that result from deleterious molecular alterations to hemoglobin and are broadly classified into two categories based on the phenotypic characteristics of these variations.[1] One of these categories includes disorders, such as sickle cell anemia, in which there is a structural defect in one of the globin subunits.[1] Thalassemia belongs to the second category of hemoglobinopathies in which there is a quantitative defect in the production of one or more of the globin subunits.[1]

In adults, hemoglobin is a heterotetramer that is comprised of the α-and β-globin subunits.[2] Each globin subunit forms a stable linkage with heme so that oxygen in the cytosol of an erythrocyte can bind reversibly to heme's iron atoms.[2] The hemoglobin tetramer $\alpha_2\beta_2$ binds and unloads oxygen in a cooperative manner, which maximizes the transport of oxygen to cells.[2] Additional gas transport functions of hemoglobin include the transport of carbon dioxide and nitric oxide.[3] Each of these physiological aspects of hemoglobin are deleteriously affected in the hemoglobinopathy disorders.

β-Thalassemia

Autosomal mutations in the gene encoding the β-globin subunit cause β-thalassemia (also known as thalassemia major or Cooley's anemia).[5] These mutations inhibit the synthesis of β-globin in erythropoietic cells.[2,4] The extent of the molecular basis for these mutations is very heterogeneous because over 200 mutations within the β-globin subunit, ranging from synonymous mutations to deletions.[1] Consequently, α-globin molecules form toxic aggregates which destroy erythroid precursors through a process called ineffective erythropoiesis.[2,4] Also, individuals with β-thalassemia suffer from anemia due to shortened red blood cell survival, hemolytic anemia.[4]

Hematopoietic Cell Transplantation

Lucarelli et al. and Angelucci et al. both have documented the literature for recent reports on outcomes of HCT from HLA-matched donors in cases of β-thalassemia.[5,8] Although stem cell sources and the risk categories of the patients vary, overall survival and thalassemia-free survival range from approximately 65% to 90 % among the numerous reports.[5,8]

Additional considerations for HCT for β-thalassemia include key issues for risk factors for transplant-related complications, transplant outcome, and conditioning regimen.[7] The major risk factors when considering HCT for β-thalassemia include age and organ dysfunction due to iron overload. Control of iron overload and related tissue damage is a significant consideration for HCT for β-thalassemia.[7] Lastly, β-thalassemia patients require an ablative conditioning regimen.[7,8]

Coding Implications

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CPT®* Codes	Description

38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor

HCPCS Codes	Description
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 posttransplant care in the global definition

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed	11/25	

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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

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Note: For Medicaid members/enrollees, 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 member/enrollees, 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.