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| Subject: Hematopoietic Stem Cell Transplantation for Sickle Cell Disease or Thalassemia Major | | Original Effective Date: 11/11/2014 |
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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP) document and provide the directive for all Medicare members.¹

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DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Hemoglobinopathy: Sickle Cell Disease and Thalassemia

Sickle cell disease (SCD) is an inherited hemoglobinopathy characterized by chronic hemolytic anemia and intermittent painful obstruction of blood vessels (vaso-occlusive crisis). The trademark feature of SCD is the presence of sickle-shaped red blood cells (RBC) on peripheral blood smear. SCD can occur in individuals of any ethnicity, but is most common in individuals of African, Caribbean, Mediterranean, Middle Eastern, and Indian ancestry. SCD occurs in approximately 1 in 500 African-American infants born in the United States therefore, screening for SCD has been incorporated into many newborn screening panels. Approximately 60% to 70% of SCD in the United States is caused by a homozygous (i.e., present on both copies of the gene) variant known as hemoglobin S [HbS]. Other forms of SCD have the variant known as

hemoglobin C [HbC]. Various types of thalassemia are also classified as an inherited hemoglobinopathy characterized by anemia that affects males and females. The disorders occur most often among people of Italian, Greek, Middle Eastern, Southern Asian, and African descent. It is estimated that 1,000 individuals in the U.S. have beta thalassemia major, the most severe form of thalassemia and the only form for which transplant is indicated. ^{5 8 30}

Stem Cell Transplantation

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor 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). HSCs are created in the bone marrow and are found in the bone marrow and peripheral blood. There is also a high concentration of HSCs in umbilical-cord blood. Hematopoietic stem-cell transplantation (HSCT) can be either autologous (using the person's own stem cells) or allogeneic (using stem cells from a donor). In allogeneic HSCT, it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed on the basis of variability at three of more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). As HLA variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease, also increase.

RECOMMENDATION ^{1-8 31 32}

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, state regulations and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Members must meet UNOS/OPTN policies and guidelines for pretransplantation evaluation and listing criteria and the diagnosis must be made by a Specialist in the Disease and or Transplant Surgeon.

Pre-Transplant Evaluation: ^{1-8 31 32} **Please see MCP-323 Pre-Transplant Evaluation for additional criteria and information.**

1. Criteria for transplant evaluation include all of the following:

- History and physical examination
- Psychosocial evaluation and clearance: [ALL]
 - No behavioral health disorder by history or psychosocial issues:
 - if history of behavioral health disorder, no severe psychosis or personality disorder
 - mood/anxiety disorder must be excluded or treated
 - member has understanding of surgical risk and post procedure compliance and follow-up required
 - Adequate family and social support
- EKG
- Chest X-ray
- Cardiac clearance in the presence of any of the following: [ONE]
 - chronic smokers
 - > 50 years age
 - those with a clinical or family history of heart disease or diabetes
- Pulmonary clearance if evidence of pulmonary artery hypertension (PAH) or chronic pulmonary disease
- Neurological exam and clearance for transplant: [ONE]
 - Normal exam by H&P

- Abnormal neurological exam with positive findings: [ONE]
 - Lumbar puncture normal cytology
 - Lumbar puncture with cytological exam abnormal: CNS disease treated prior to clearance
- ☐ Performance Status : [ONE]
 - Karnofsky score 70-100%; or
 - Eastern Cooperative Oncology Group (ECOG) grade 0-2
- ☐ Lab studies:
 - *Complete blood count, Kidney profile (blood urea nitrogen, creatinine), electrolytes, calcium, phosphorous, albumin, liver function tests, Coagulation profile (prothrombin time, and partial thromboplastin time)
 - *Serologic screening for HIV, Epstein Barr virus (EBV), Hepatitis virus B (HBV), and Hepatitis C(HCV), cytomegalovirus (CMV), RPR and/or FTA:
 - If HIV positive all of the following are met:
 - CD4 count >200 cells/mm-3 for >6 months
 - HIV-1 RNA undetectable
 - On stable anti-retroviral therapy >3 months
 - No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
 - If abnormal serology need physician plan to address and/or treatment as indicated
 - UDS (urine drug screen) if patient is current or gives a history of past drug abuse
- ☐ *Colonoscopy (if indicated or if patient is 50 ≥ older should have had an initial screening colonoscopy, after initial negative screening requires follow up colonoscopy every ten years) with complete workup and treatment of abnormal results as indicated
- ☐ *GYN examination with Pap smear (if indicated or > age 18) with in the last three year with complete workup and treatment of abnormal results as indicated

Within the last 12 months:

- ☐ Dental examination or oral exam showing good dentition and oral care or no abnormality on panorex or plan for treatment of problems pre or post-transplant
- ☐ *Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated
- ☐ *PSA if history of prostate cancer or previously elevated PSA with complete workup and treatment of abnormal results as indicated

**Participating Centers of Excellence may waive these criteria*

Criteria for Hematopoietic Allogeneic Stem Cell transplantation (HSCT) Transplantation: ^{1-8 31-33}

1. ***Hematopoietic Allogeneic stem-cell transplantation (HSCT) ablative or non-myeloablative*** from a human leukocyte antigen (HLA)-matched donor ¹⁰ (i.e., at least six out of eight match of the HLA-A, HLA-B, HLA-C and HLA-DRB1 markers) for the treatment of a child or adolescent at increased risk of complications of sickle cell disease (SCD) or thalassemia major when ANY of the following criteria are met:

- ☐ All pre-transplant criteria are met; and
- ☐ In children and adolescents with SCD who are ≤ 16 years of age who have one or more of the following risk factors or complications:

- Stroke or central nervous system (CNS) event lasting longer than 24 hours
 - Progressive neurologic deterioration (e.g., abnormal cerebral MRI and arteriogram) and impaired neuropsychiatric testing
 - Recurrent acute chest syndrome or Stage I or II sickle lung disease
 - Recurrent vaso-occlusive painful episodes
 - Sickle nephropathy [glomerular filtration rate (GFR) 30-50 percent of predicted normal]
 - Osteonecrosis of multiple joints
- In children and adolescents with thalassemia major who are ≤ 16 years of age and have all of the following risk factors or complications:
- deterioration with conventional treatments including transfusions, splenectomy, and deferoxamine;

AND

The requesting transplant recipient should not have any of the following **absolute contraindications**:⁵

- Cardiac, pulmonary, and nervous system disease that cannot be corrected and is a prohibitive risk for surgery
- Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer)
- Systemic and/or uncontrolled infection
- AIDS (CD4 count < 200 cells/mm³)
- Unwilling or unable to follow post-transplant regimen
 - Documented history of non-compliance
 - Inability to follow through with medication adherence or office follow-up
- Chronic illness with one year or less life expectancy
- Severe irreversible extra renal disease
- Limited, irreversible rehabilitation potential
- Active untreated substance abuse issues, requires documentation supporting free from addiction for minimally 6 months if previous addiction was present
- No adequate social/family support

The requesting transplant recipient should be evaluated carefully and potentially treated if the following **relative contraindications** are present:

- Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation, this includes the following:
 - Smoking, documentation supporting free from smoking for 6 months
 - Active peptic ulcer disease
 - Active gastroesophageal reflux disease
 - CVA with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months
 - Obesity with body mass index of >30 kg/m² may increase surgical risk
 - Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hepatologist
 - Gall bladder disease requires ultrasound of the gall bladder with treatment prior to transplantation

Criteria for Subsequent Hematopoietic Stem Cell Transplantation:

2. A second or repeat ***Hematopoietic Allogeneic stem cell transplantation*** (*ablative or non-myeloablative*) may be authorized only one time when all of the above criteria for transplant have been met and any of the following:
[ONE]

- primary graft failure indicated by no signs of engraftment* by 42 days after the transplant; or
- failure to engraft*

**Note: Engraftment is defined as the first 3 consecutive days on which the absolute neutrophil count (ANC) exceeds $5 \times 10^9/L$ or $> ANC500$ at any time after transplantation.⁷*

Criteria for Donor Lymphocyte Infusion (DLI): ³¹

3. ***Donor lymphocyte infusion (DLI), collection and cryopreservation*** may be authorized following a medically necessary allogeneic hematopoietic stem cell transplant:

- For incomplete chimerism and disease relapse in the setting of incomplete chimerism (defined as incomplete donor stem cell grafting in the recipient's bone marrow); and
- Donor lymphocytes must be collected from the original hematopoietic stem cell donor

CONTINUATION OF THERAPY

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

- If Molina Healthcare has authorized prior requests for transplantation, the following information is required for medical review: [ALL]
 - o Presence of no absolute contraindication as listed above;
 - o History and physical within the last 12 months;
 - o Kidney profile within the last 12 months;
 - o Cardiac update if history of cardiac disease within two years (≥ 50 years of age);
 - o Psychosocial evaluation or update within the last 12 months;
 - o Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.
- If authorized prior requests for transplantation were obtained from another insurer, the following information is required for medical review: [ALL]
 - o Authorization letter/documentation from previous insurer;
 - o Presence of no absolute contraindication as listed above;
 - o History and physical within the last 12 months;
 - o Cardiac update if history of cardiac disease within two years (≥ 50 years of age);
 - o Psychosocial evaluation or update within the last 12 months;
 - o Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

LIMITATIONS 1-8 31-33

1. Allogeneic (ablative or non-myeloablative) stem cell transplantation when the above criteria are not met.

2. A second or repeat allogeneic (ablative or non-myeloablative) transplant due to persistent, progressive or relapsed disease.
3. Autologous stem cell transplantation
4. Hematopoietic stem cell collection, storage and freezing for a future unplanned transplant

SUMMARY OF MEDICAL EVIDENCE¹⁰⁻³⁰

The published, peer-reviewed scientific literature supports the safety and effectiveness of allogeneic HSCT for the treatment of SCD and Thalassemia major (TM) in selected individuals and consists of systematic reviews,¹¹⁻¹³ retrospective and prospective multi-center clinical studies and case series.¹³⁻²³ Several studies evaluated up to 485 SCD & TM symptomatic patients, the majority of whom received donor allografts from siblings who were human leukocyte antigen (HLA) identical. The results from these series were similar, with overall survival rates ranging from 92%–94% and event-free survival from 82%–86% with a median follow-up ranging from 0.9–17.9 years.¹⁴⁻²⁴

Improved outcomes have not been demonstrated for autologous HSCT compared with conventional chemotherapy in individuals with SCD & TM therefore the role of autologous HSCT for this indication has not been established. Clinical trials are evaluating the role of unrelated donor HCT in treating severe SCD & TM and enrolling children with a history of severe symptoms manifesting as strokes, frequent pain crises, or acute chest syndrome. Experience with myeloablative HCT in older teenagers and adults with SCD & TM is insufficient and the role for this age group has not been established. A summary of the most relevant medical evidence is outlined below.

Outcomes

The largest case series analyzed the outcomes of 485 patients with thalassemia major (TM) or sickle cell disease (SCD) receiving HLA-identical sibling cord blood transplantation (CBT, n = 96) or bone marrow transplantation (BMT, n = 389). Compared with patients given BMT, CBT recipients were significantly younger (median age 6 vs 8 years, P = .02), and were treated more recently (median year 2001 vs 1999, P < .01). A higher proportion of patients with TM belonging to classes II-III of the Pesaro classification received BMT (44%) compared with CBT (39%, P < .01). In comparison with patients receiving BMT (n = 259, TM; n = 130, SCD), those given CBT (n = 66, TM; n = 30, SCD) had slower neutrophil recovery, less acute graft-versus-host disease (GVHD) and none had extensive chronic GVHD. With a median follow-up of 70 months, the 6- year overall survival was 95% and 97% after BMT and CBT, respectively (P = .92). The 6-year disease-free survival (DFS) was 86% and 80% in TM patients after BMT and CBT, respectively, whereas DFS in SCD patients was 92% and 90%, respectively. The cell dose infused did not influence outcome of patients given CBT. In multivariate analysis, DFS did not differ between CBT and BMT recipients. Patients with TM or SCD have excellent outcomes after both HLA identical sibling CBT and BMT.¹⁴

The outcomes of 50 consecutive children with severe SCD that received HSCT between November 1988 and April 2013 were reported. The stem cell source was bone marrow (n = 39), cord blood (n = 3), bone marrow and cord blood (n = 7) and peripheral blood stem cells (n = 1). All patients had >1 severe manifestation: 37 presented with recurrent vaso-occlusive crises/acute chest syndrome, 27 cerebral vasculopathy and 1 nephropathy. The conditioning regimen consisted of busulfan +cyclophosphamide (BuCy) before November 1991 and BuCy + rabbit antithymocyte globulin after that date. Since 1995, all patients have been treated with hydroxycarbamide (HC) prior to transplantation for a median duration of 27 years. Median age at transplantation and median follow-up was 83 and 77 years, respectively. Acute graft-versus-host disease (GVHD) and chronic GVHD were observed in 11 and 10 patients, respectively. An excellent outcome was achieved, with 8-year overall survival and event-free survival (EFS) rates of 941% and 856%, respectively. Since HC introduction, no graft failure occurred and EFS reached 974%. Prior treatment with HC may have contributed to successful engraftment.¹⁸

Arnold et al. (2017), performed a retrospective study of children transplanted for sickle cell disease in the USA during 2000-2013 using two large databases. Univariate and Cox models were used to estimate associations of demographics, sickle cell disease severity, and transplant-related variables with mortality and chronic graft-versus-host disease. Among 161 patients with a 2-year overall survival rate of 90% (95% confidence interval [CI] 85-95%) mortality was significantly higher in those who underwent late transplantation versus early (hazard ratio (HR) 21, 95% CI 2.8-160.8, P=0.003) and unrelated compared to matched sibling donor transplantation (HR 5.9, 95% CI 1.7-20.2, P=0.005). Chronic graft versus host disease was significantly more frequent among those transplanted late (HR 1.9, 95% CI 1.0-3.5, P=0.034) and those who received an unrelated graft (HR 2.5, 95% CI 1.2-5.4; P=0.017).²⁹

CODING INFORMATION: THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS A COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

| CPT | Description |
|---------------------------------|--|
| Collection Codes | |
| 38205 | Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic |
| 38206 | Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous |
| 38230 | Bone marrow harvesting for transplantation; allogeneic |
| 38232 | Bone marrow harvesting for transplantation; autologous |
| Cell Processing Services | |
| 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 |
| 38211 | Transplant preparation of hematopoietic progenitor cells; tumor 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 |
| Cell infusion codes | |
| 38240 | Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic |
| 38241 | Bone marrow or blood-derived peripheral stem cell transplantation; autologous |
| 38242 | Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions |
| 38243 | Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic hematopoietic cellular transplant boost |

| HCPCS | 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 |

| ICD-10 | Description: [For dates of service on or after 10/01/2015] |
|----------------|--|
| D56.0-D56.9 | Thalassemia |
| D57.00-D57.819 | Sickle-cell disease |

RESOURCE REFERENCES

Government Agency

- Centers for Medicare & Medicaid Services. NCD for Stem Cell Transplantation (Formerly 110.8.1) 110.23. Effective date 1/27/2016. Accessed at: <http://www.cms.gov/medicare-coverage-database/>

Professional Society Guidelines

- American Society for Blood and Marrow Transplantation (ASBMT). Policy Statements. Accessed at: <https://www.astct.org/advocate/policy-statements>
- American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. *Blood Adv* (2020) 4 (8): 1554–1588. Accessed at: <https://ashpublications.org/bloodadvances/article/4/8/1554/454384>
- Eastern Cooperative Oncology Group (ECOG) Performance Status. Accessed at: http://www.ecog.org/general/perf_stat.html
- National Heart, Lung and Blood Institute.
 - What are thalassemias? 2012. Accessed at: <http://www.nhlbi.nih.gov/health/health-topics/topics/thalassemia/>
 - The management of sickle cell disease, 4th ed. NIH Publication 02-2117. Jun 2002. Accessed at: http://www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf
 - Evidence-Based Management of Sickle Cell Disease Expert Panel Report, 2014. Accessed at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf
- National Institute of Health. Evidence-Based Management of Sickle Cell Disease Expert Panel Report, 2014. Available at: <https://www.nhlbi.nih.gov/sites/www.nhlbi.nih.gov/files/sickle-cell-disease-report.pdf>
- National Marrow Donor Program® (NMDP) and the American Society for Blood and Marrow Transplantation (ASBMT) referral guidelines: Recommended Timing for Transplant Consultation. Accessed at: http://marrow.org/Physicians/When_to_Transplant/Referral_Guidelines.aspx
- National Marrow Donor Program® (NMDP):
 - Patient Eligibility for HCT. Accessed at: <https://bethematchclinical.org/Transplant-Indications-and-Outcomes/Eligibility/>
 - SCD and Thalassemia Transplant Outcomes. Accessed at: http://marrow.org/Physicians/When_to_Transplant/Outcomes_by_Disease.aspx
 - HLA Matching Requirements. Accessed at: http://marrow.org/Patient/Transplant_Process/Search_Process/HLA_Matching_Finding_the_Best_Donor_or_Cord_Blood_Unit.aspx
 - National Bone Marrow Donor Program. Measuring Engraftment. Accessed at: http://marrow.org/Patient/Transplant_Process/Days_0-30/Measuring_Engraftment.aspx
- Sickle Cell Disease Association of America (SCDAA). About sickle cell disease. Copyright © 2019 Sickle Cell Disease Association of America, Inc. Accessed at: <http://www.sicklecelldisease.org/>

Peer Reviewed Literature

- C Mackall, T Fry, R Gress, K Peggs, J Storek and A Toubert. Background to hematopoietic cell transplantation, including post-transplant immune recovery. *Bone Marrow Transplant* 44: 457-462; doi:10.1038/bmt.2009.255
- Oringanje C, Nemecek E, Oniyangi O. Hematopoietic stem cell transplantation for people with sickle cell disease. *Cochrane Database Syst Review*. 2013 May 31;(5):CD007001
- Kavanagh P.L., Sprinz P.G., Vinci S.R., Bauchner H., Wang C.J. Management of children with sickle cell disease: A comprehensive review of the literature. *Pediatrics*. 128 (6) (pp e1552-e1574), 2011.

13. Jagannath VA, Fedorowicz Z, Al Hajeri A, Hu N, Sharma A. Hematopoietic stem cell transplantation for people with β -thalassaemia major. *Cochrane Database of Systematic Reviews* 2011, Issue 10. Art. No.: CD008708. DOI: 10.1002/14651858.CD008708.pub2
14. Locatelli F, Kabbara N, Ruggeri A, et al. Outcome of patients with hemoglobinopathies given either cord blood or bone marrow transplantation from an HLA-identical sibling. *Blood*. 2013; 122(6):1072-10
15. Bernaudin, F, Socie, G, Kuentz, M, et al. Long-term results of related myeloablative stem-cell transplantation to cure sickle cell disease. *Blood*. 2007 Oct 1;110(7):2749-56. PMID: 17606762
16. Walters, MC, Patience, M, Leisenring, W, et al. Bone marrow transplantation for sickle cell disease. *N Engl J Med*. 1996 Aug 8;335(6):369-76. PMID: 8663884
17. Walters, MC, Storb, R, Patience, M, et al. Impact of bone marrow transplantation for symptomatic sickle cell disease: an interim report. Multicenter investigation of bone marrow transplantation for sickle cell disease. *Blood*. 2000 Mar 15;95(6):1918-24. PMID: 107068578.
18. Dedeken L, Le PQ, Azzi N et al. Haematopoietic stem cell transplantation for severe sickle cell disease in childhood: a single centre experience of 50 patients. *Br J Haematol*. 2014 May ;165(3):402-8. doi: 10.1111/bjh.12737. Epub 2014 Jan 16
19. Bhatia M, Walters, MC. Hematopoietic cell transplantation for thalassemia and sickle cell disease: past, present and future. *Bone Marrow Transplant*. 2008 Jan;41(2):109-17. PMID: 18059330.
20. Boulad F, Giardina P, Gillio A, Kernan N, Small T, Brochstein J et al. Bone marrow transplantation for homozygous beta-thalassemia. The Memorial Sloan-Kettering Cancer Center experience. *Ann N Y Acad Sci* 1998; 850: 498–502.
21. Lee YS, Kristovich KM, Ducore JM, Vichinsky E, Crouse VL, Glader BE et al. Bone marrow transplant in thalassemia. A role for radiation? *Ann N Y Acad Sci* 1998; 850: 503–505.
22. Mentzer WC, Cowan MJ. Bone marrow transplantation for beta-thalassemia: the University of California San Francisco experience. *J Pediatr Hematol Oncol* 2000; 22: 598–601.
23. Walters MC, Hardy K, Edwards S, Adamkiewicz T, et al. Pulmonary, gonadal, and central nervous system status after bone marrow transplantation for sickle cell disease. *Biology of Blood & Marrow Transplantation*. Feb 2010;16(2):263-72.
24. Angelucci E, Matthes-Martin S et al. Hematopoietic stem cell transplantation in thalassemia major and sickle cell disease: indications and management recommendations from an international expert panel. *Haematologica*. May 2014; 99(5):811. Accessed at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4008115/>
25. Bhatia M, Sujit S. Hematopoietic stem cell transplantation in sickle cell disease: patient selection and special considerations. *J Blood Med*. 2015; 6: 229–238.
26. Chevret S, Verlhac S, Ducros-Miralles E et al. Design of the DREPAGREFFE trial: A prospective controlled multicenter study evaluating the benefit of genoidentical hematopoietic stem cell transplantation over chronic transfusion in sickle cell anemia children detected to be at risk of stroke by transcranial Doppler (NCT 01340404). *Contemp Clin Trials*. 2017 Nov;62:91-104.
27. Kassim AA, Sharma D. Hematopoietic stem cell transplantation for sickle cell disease: The changing landscape. *Hematol Oncol Stem Cell Ther*. 2017 Jun 15. pii: S1658-3876(17)30044-4.
28. Wiebking V, Hütker S et al. Reduced toxicity, myeloablative HLA-haploidentical hematopoietic stem cell transplantation with post-transplantation cyclophosphamide for sickle cell disease. *Ann Hematol*. 2017 Aug;96(8):1373-1377.
29. Arnold SD, Brazauskas R, He N et al. Clinical risks and healthcare utilization of hematopoietic cell transplantation for sickle cell disease in the USA using merged databases. *Haematologica*. 2017 Nov;102(11):1823-1832.
30. Oringanje C, Nemecek E, Oniyangi O. Hematopoietic stem cell transplantation for people with sickle cell disease. *Cochrane Database Syst Rev*. 2016 May 19;(5):CD007001. doi: 10.1002/14651858.CD007001.pub4.

Other Resources

31. DynaMed LLC [website]. EBSCO Publishing 1998-2020. Sickle Cell Disease. 2020.
32. UpToDate: [website]. Waltham, MA: Walters Kluwer Health; 2020.
 - Kahn S, Rogers G. Hematopoietic cell transplantation in sickle cell disease.
 - Field J, Vichinsky E, Debaun M. Overview of the management and prognosis of sickle cell disease.
 - Rogers G. Hydroxyurea and other disease-modifying therapies in sickle cell disease.

- Negrin C. Immunotherapy for the prevention and treatment of relapse following hematopoietic cell transplantation.
 - Deeg HJ, Sandmaier B. Determining eligibility for allogeneic hematopoietic cell transplantation.
 - Chao NG. Selection of an umbilical cord blood graft for hematopoietic cell transplantation.
33. Hayes a Tract Manager Company. Winifred Hayes Inc. Lansdale PA.
- HTA: Allogeneic Hematopoietic Stem Cell Transplantation for Sickle Cell Disease in Children and Young Adults. Feb, 2016. Updated May 2020.
34. Peer Review: Policy reviewed by AMR practicing physician board certified Pediatrics, Pediatric Hematology/Oncology. 11/1/17

Review/Revision History:

11/11/14: New Policy

6/2/15: Updated pre-transplant criteria, continuation of therapy, absolute and relative contraindications and coding sections.

9/15/16: Policy reviewed, no changes

12/13/17: The clinical criteria have not changed. Summary of medical evidence, professional guidelines and reference sections were updated.

9/13/18 & 9/18/19: Policy reviewed, no changes

9/16/20: Policy reviewed, no changes. Updated references and guidelines.