Stem-Cell Transplantation for Sickle Cell Disease and Thalassemia Major

**Coverage Policy**

Myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) from a human leukocyte antigen (HLA)-matched donor (i.e., at least five of six match of the HLA-A, HLA-B, and HLA-DRB1 antigens) is considered medically necessary for the treatment of a child or young adult at increased risk of complications of sickle cell disease (SCD) or thalassemia major.

Non-myeloablative allogeneic HSCT for a child or young adult with SCD or thalassemia major is considered experimental, investigational or unproven.

**Overview**

This Coverage Policy addresses allogeneic hematopoietic stem-cell transplantation (HSCT) for the treatment of sickle cell disease (SCD) or thalassemia major. SCD and thalassemia are genetic diseases.

SCD is a group of disorders that affects hemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body. People with this disorder have sickle or crescent-shaped red blood cells. This distorted
shape can deprive tissues and organs of oxygen-rich blood, leading to organ damage, high blood pressure and increased pressure in the lungs, which can lead to heart failure.

Thalassemia major is a blood disorder that reduces the production of hemoglobin. Low levels of hemoglobin lead to a lack of oxygen, a severe shortage of red blood cells, resulting in life-threatening anemia and an increased risk of developing blood clots.

Allogeneic HSCT involves taking hematopoietic stem cells that can regenerate all the blood cells normally produced in the bone marrow from the bone marrow or blood of a donor and infusing them into a person with SCD or thalassemia major. Allogeneic HSCT represents the only possibility of a cure for SCD or thalassemia major by providing donor hematopoietic stem cells with normal copies of the hemoglobin genes to the transplant recipient.

General Background

Hemoglobinopathies are a group of rare, inherited disorders involving abnormal structure of the hemoglobin molecule. Several hundred unusual hemoglobins have been identified. Clinically significant variants include hemoglobin S-C disease, sickle cell anemia, various types of thalassemia, hemoglobin C, and hemoglobin E. (National Institutes of Health [NIH], 2013; Chiu, 2005; Sickle Cell Disease Association of America [SCDAA], 2014).

Stem-Cell Transplantation

Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into an individual. HSC transplantation (HSCT) can be either autologous (using the individual'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 or 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. Although considered a standard approach for the treatment of malignant disease, HSCT with the use of haploidentical donors remains a subject of ongoing clinical trials. There are limited data to support the safety and effectiveness of a haploidentical donor for the treatment of sickle cell disease or thalassemia major.

Sickle Cell Disease (SCD): SCD encompasses many sickling syndromes caused by abnormal sickle hemoglobin. The most common are sickle cell anemia (Hb SS), sickle-hemoglobin C disease (Hb SC), sickle-beta plus thalassemia, and sickle-beta zero thalassemia (NIH, 2013). The disease follows a variable clinical course which may include complications such as severe anemia, painful sickle cell crises, organ damage due to iron overload, acute chest syndrome, refractory pain, stroke, and premature death. Accepted treatment options include chronic blood transfusions, hydroxyurea, and allogeneic HSCT for children and young adults at risk for complications of the disease.

Gluckman et al. (2017) reported a retrospective survey of results of HSCT for 1000 recipients of HLA-identical sibling transplants performed between 1986 and 2013 at 106 centers in 23 countries and reported to the European Society for Blood and Marrow Transplantation, Eurocord, and the Center for International Blood and Marrow Transplant Research. The primary endpoint was event-free survival. The median age at transplantation was nine years, and median follow-up was > 5 years. Median range for children was 8.3 years (0.3-16) and for adults was 19.3 years (16-54.4). Eighty-seven percent of patients received a myeloablative conditioning regimen; thirteen percent received reduced-intensity conditioning regimens. The five-year OS was 95% and 81%, respectively, for patients younger than 16 years and those aged 16 years or older (p<.001); the corresponding EFS was 93% and 81% (p<.001). The five-year probability of GVHD-free survival was 86% and 77%, respectively, for patients younger than 16 years and 16 years or older (p<.001). Multivariate analysis results confirmed the significant association of age at HSCT; EFS and OS were both lower with increasing age. For every one-year increment in age, there was a 9% increase in the hazard ratio (HR) for treatment failure (i.e., graft failure or death). Similarly, for every one-year increment in age, there was a 10% increase in the HR for
death. The authors note transplantation of grafts from HLA-identical siblings offers excellent five-year survival, nonetheless; it is also important to study the effects of transplantation in the long term and to develop prospective trials of comparable patient cohorts to determine the relative merits of transplantation versus supportive care, especially in older patients with severe SCD.

**Myeloablative Allogeneic HSCT:** Myeloablative allogeneic HSCT is the only potentially curative treatment option for selected individuals with sickle cell disease or thalassemia major (Novelli, 2011; Bhatia, 2008; Krishnamurti, 2008). HSCT involves replacing the deformed red blood cells and the cells that produce them with normal cells from a healthy donor. Research to date has demonstrated that successful engraftment of normal donor hematopoietic stem cells prevents additional pathological effects of SCD. Full donor chimerism is not necessary to achieve this effect (Iannone, 2005; Krishnamurti, 2008).

The optimal timing for marrow transplantation in the course of SCD remains uncertain, in part, because of the unpredictable nature and clinical heterogeneity of the disease. Patient selection criteria continue to evolve. Due to complications of disease and transplant-related morbidity and mortality, a child or young adult is generally considered the most appropriate candidate for transplantation. Indications for HSCT have been derived from prognostic factors derived from studies of the natural history of SCD. The most common indications for which patients with SCD have undergone HSCT are a history of stroke, recurrent acute chest syndrome, or frequent vaso-occlusive episodes (Novelli, 2011). Children and younger adults who have severe complications (e.g. stroke, recurrent acute coronary syndrome [ACS], refractory pain) and have a human-leukocyte antigen (HLA)-matched donor are the best candidates for transplantation (Panepinto, 2007).

Current research is focused on improving the applicability of HSCT to a greater proportion of patients with SCD by the development of novel conditioning regimens minimizing myeloablation and the use of novel sources of hematopoietic stem cells such as umbilical cord blood (Novelli, 2011).

**Literature Review**

Although data are not robust, myeloablative allogeneic HSCT is considered an appropriate treatment option for selected children and young adults at high risk of complications of SCD. There are scarce data in the published, peer-reviewed scientific literature regarding safety and effectiveness in the adult population and at this time the role of myeloablative allogeneic HSCT for has not been established for this indication.

Oringanje et al. (2016) performed a systematic review to determine whether stem-cell transplantation can improve survival, and prevent symptoms and complications associated with sickle cell disease. Data from randomized controlled and quasi-randomized studies were lacking; therefore, no conclusions could be made. The authors note that this systematic review identified the need for a multicenter randomized controlled trial assessing the benefits and possible risks of HSCT comparing sickle status and severity of disease in an individual with SCD.

However, several case series, retrospective reviews, and registry analyses have demonstrated improved overall- and event-free survival with allogeneic HSCT, primarily in an individual ≤30 years (Dallas, 2013; Bernauldin, 2007; Panepinto, 2007; Locatelli, 2005). Five and six-year probabilities of disease-free-(DFS), and overall survival (OS) were 85%–86%, and 93%–97%, respectively (Dallas, 2013; Novelli, 2011; Bernauldin, 2007); Panepinto, 2007 [median age 10 years]. In the retrospective analysis by Dallas et al. (2013) involving 22 children with sickle cell disease who underwent an allogeneic HSCT. Eligible study participants were up to 22 years (median 11 years for matched related donor recipients and nine years for haploidentical donor graft recipients). Median follow-up was 9.0 years, with an OS of 93% and a recurrence/graft failure rate of 0%, for those using matched-related donors. For those undergoing haploidentical allogeneic HSCT, median follow-up was 7.4 years, with an OS of 75%, DFS of 38%, and disease recurrence of 38%. Although limited by uncontrolled study design and small patient numbers, data suggest an improved overall survival (OS) with allogeneic hematopoietic stem-cell transplantation (HSCT).

**Non-Myeloablative Allogeneic HSCT for SCD:** Toxicity of myeloablative conditioning regimens and the finding that mixed chimerism can cure SCD have prompted recent studies using reduced toxicity conditioning regimens that do not cause ablation of hematopoiesis. At present, study populations include very small numbers of adults.
and children who have evidence of organ damage from vaso-occlusion or iron overload as a result of chronic transfusion therapy.

Mortality related to graft-versus-host disease and graft rejection continues to be a complication related to this therapy. Published reports have confirmed improved safety, but the majority of these transplants are unsuccessful because of graft failure (Horwitz, 2007). Although investigations are continuing, it has been difficult to identify a regimen that is sufficiently immunosuppressive to ensure stable engraftment of donor cells while continuing to meet the objective of reduced toxicity.

**Literature Review**

The ability to draw conclusions regarding the effectiveness of this therapy is limited by small study size, use of heterogeneous conditioning regimens, and study design. Although promising and a subject of ongoing research, the role of nonmyeloablative conditioning and allogeneic HSCT has not yet been established for this indication.

Although of prospective design, more recent studies are phase I/II trials. Outcomes of several uncontrolled trials suggest that donor chimerism is possible in a majority of patients (Saraf, 2015; Bhatia, 2014; Hsieh, 2014; Krishnamurti, 2008; Horwitz, 2007; Horan, 2005; Iannone, 2003). However, controlled clinical trial data are lacking, study populations are very small, and long-term effect on overall health outcomes is unknown.

Data reported to the European Group for Blood and Marrow Transplantation hemoglobinopathy database (Shenoy et al, 2017) reflect OS and EFS rates of 95% and 92%, respectively. Results observed after a reduced-intensity conditioning applied in children and a nonmyeloblative regimen in adults were similar to results after myeloablative conditioning, with OS and EFS rates of 90.7% and 87%, respectively.

King et al. reported results of a trial of 52 children (median age 11.5 years) with symptomatic SCD (n=43) or transfusion dependent thalassemia (n=9) who received matched sibling donor marrow, marrow and cord product, or cord blood allografts following reduced intensity conditioning. Probabilities of OS and EFS at a median of 3.42 years were 94.2% and 92.3% for the group, 93% and 90.7% for SCD, and 100% and 100% for thalassemia, respectively. Treatment-related mortality was noted in three (5.7%) recipients with SCD, all 17–18 years of age and related to GVHD. Donor chimerism at 2 years was available in 35 patients. Twelve patients who had mixed chimerism at one year maintained this status (28–89% donor) at two years. No patient had recurrence of disease symptoms, transfusion requirement, or hemoglobin analysis suggestive of hemoglobinopathy recurrence. Transfusion independence was uniformly achieved by day 100 post-HCT in all recipients except one patient with graft rejection. Acute and chronic GVHD was noted in 23% and 13%, respectively, with 81% of recipients off immunosuppression by one year. All patients who engrafted were transfusion independent; no strokes or pulmonary complications of SCD were noted, and pain symptoms subsided within 6 months post-transplant.

Saraf et al. (2016) analyzed results of a prospective phase I/II observational study of 13 patients with sickle cell disease who underwent nonmyeloablative allogeneic HSCT with alemtuzumab and low-dose irradiation. Patient age ranged from 17 to 40 years, median age 28.6 years. Two patient-donor pairs were mismatched for the major ABO blood types. The primary endpoint was the engraftment rate at one year after HSCT. Secondary endpoints included transplantation-related toxicity, acute and chronic graft-versus-host disease (GVHD), SCD-related complications, quality of life (QoL) and overall and disease-free survival. At one year after HSCT, 12 of the 13 patients (92%) maintained stable donor chimerism. There was no transplantation-related mortality. Hemoglobin values improved from median baseline values of 7.8 g/dL and 8.1 g/dL in women and men, respectively, to 12.4 g/ in women and 15.0 g/dL in men at one year after HSCT (p <.0001). Disease-free survival was 92% at a median follow up of 22 months. No patients developed acute or chronic GVHD and four patients were titrated off sirolimus after HSCT. Nine patients completed the QoL assessments at both the pre-HSCT and one-year post-HSCT time points. At one year, the mean scores of the patients in all domains were within one half standard deviation of the population mean scores, except for physical functioning. A significant effect was observed for general health, vitality social functioning and the overall preference-based summary score. Although limitations include uncontrolled study design and small study population, primary and secondary endpoints were met.

Bhatia et al. (2014) reported results of a prospective trial involving 18 children with SCD (median age 8.9 years, range 2.3-20.2) who underwent reduced-toxicity conditioning HLA-matched sibling donor allogeneic HSCT. The median follow-up time was 1065.5 days for all patients. The incidence of grade II–IV acute GVHD was 17% (n =
3) and of grade III–IV acute GVHD was 11% (n = 2). The incidence of chronic GVHD was 11% (n = 2). Two-year EFS and OS were 100%. Neurological, pulmonary and cardiovascular function were stable or improved at two years. All but one recipient had sustained whole blood and erythroid donor chimerisms >85% and stabilization or improvement in organ function. The authors noted that certain patients in this study did have relatively few complications before transplantation and did not satisfy the more traditional criteria for severe disease.

Hsieh et al. (2014) reported outcomes of a phase I/II prospective trial of 30 patients aged 16-65, median age 28.5 years. Participants had severe sickle cell disease or thalassemia and underwent nonmyeloablative allogeneic HSCT with HLA-matched sibling donors. The primary endpoint was defined as full donor-type hemoglobin at one year after transplantation for patients with sickle cell disease and transfusion independence for patients with thalassemia. Secondary endpoints were the level of donor leukocyte chimerism; incidence of acute and chronic graft-vs-host disease; and sickle cell and thalassemia disease-free survival, immunologic recovery, and changes in organ function. Twenty-nine patients survived a median 3.4 years. There was no nonrelapse mortality. Twenty-six patients (87%) had long-term stable donor engraftment without acute or chronic graft-versus-host disease. Fifteen engrafted patients discontinued immunosuppression medication with continued stable donor chimerism and no graft-versus-host disease. The normalized hemoglobin and resolution of hemolysis among engrafted patients were accompanied by stabilization in brain imaging, a reduction of echocardiographic estimates of pulmonary pressure, and allowed for phlebotomy to reduce hepatic iron. The mean annual hospitalization rate was 3.23 the year prior to transplantation compared with 0.63, 0.19 and 0.11 the first, second and third years, respectively, following transplantation. For patients taking long-term narcotics, mean use per week decreased from 639 mg of intravenous morphine-equivalent dose the week of transplantation compared with 140 mg six months after transplantation. Six participants who were taking narcotics long-term without irreversible bone or joint damage were successfully weaned from narcotics. There were 38 serious adverse events, including pain, infection, and sirolimus-related toxic effects. The authors note further follow-up is required to assess longer-term clinical outcomes, adverse events, and transplant tolerance. Study limits include uncontrolled study design, small study populations and short-term follow-up.

Krishnamurti (2008) evaluated outcomes for seven patients (median age eight years) with severe SCD who underwent allogeneic HSCT with reduced-intensity conditioning. At one year post transplantation six of seven patients had mixed donor chimerism. At a follow-up of 2-8.5 years after transplantation, all patients were alive, off immunosuppression, and six of seven patients had no laboratory or clinical evidence of disease.

Horan et al. (2005) reported the results of four consecutive patients who received allogeneic HSCT with non-myeloablative conditioning. Three patients had SCD (two patients had Hb SS; one patient had Hb C), and one patient had thalassemia major. Donors were human leukocyte antigen (HLA)-identical siblings in all cases. At three months post-transplantation, all patients had evidence of donor myeloid chimerism (range 15–100%); however, post-transplantation immunosuppression was discontinued and graft rejection occurred in three recipients. At 27 months’ follow-up, one patient was doing well, with full donor chimerism. One patient received a second HSCT for graft failure and died at 52 days post-HSCT due to pneumonia and intractable heart failure. The other patients remained alive but without significant donor chimerism.

**Thalassemia**: Thalassemia is a hereditary anemia resulting from defects in hemoglobin production. These defects result in low levels of hemoglobin being produced and excessive destruction of red blood cells. There are two types of thalassemia, alpha and beta, depending on which of the two hemoglobin chains is involved. Alpha and beta thalassemia have both mild (i.e., minor) and severe (i.e., major) forms; the severity of the disease depends on the number and combination of genes affected. Because individuals with thalassemia minor variants have few physical symptoms and a normal lifespan is expected, HSCT is not considered an appropriate treatment option.

The severe form of this disease is known as beta thalassemia major, Cooley’s anemia, thalassemia major or Mediterranean anemia. Thalassemia major requires frequent, lifelong blood cell transfusions and folate supplements; the effects of iron overload may damage the heart, liver and endocrine systems. Without treatment, children with the severe form of the disease usually do not live beyond early childhood; however, individuals with successfully treated thalassemia may live until their forties or beyond (National Heart, Lung, and Blood Institute [NHLBI], 2012).
Myeloablative Allogeneic Hematopoietic Stem-Cell Transplantation (HSCT) for Thalassemia: Allogeneic HSCT is considered a potentially curative therapy for selected individuals with thalassemia major who have an appropriate donor (Holstein, 2011; Hongeng, 2006; Jaing, 2005). Data strongly suggest that the optimal timing of HSCT of an individual with a human leukocyte antigen (HLA)-identical sibling donor is at a very early age (Yesilipek, 2007).

HSCT is associated with a non-negligible risk of transplantation-related mortality and morbidity which must be taken into account, considering the relevant improvements achieved with conventional therapy (Locatelli, 2005). The outcome of allogeneic HSCT using an HLA-identical family donor is largely dependent on the age of the recipient as well as on pretransplant parameters reflecting the degree of organ damage from iron overload (Resnick, 2007). As with SCD, patient selection criteria continue to evolve. A child or young adult is generally considered the most appropriate candidate for transplantation due to preexisting complications and risk of transplant-related morbidity and mortality. Results with HSCT are generally better if no iron overload or organ damage is present and the patient has received a minimal number of erythrocyte transfusions (Smiers, 2010).

Literature Review
Although data are not robust, myeloablative allogeneic HSCT is potentially curative for thalassemia major and is an accepted treatment option for selected children and young adults. However, there are scarce data in the published peer-reviewed scientific literature regarding the safety and effectiveness of myeloablative HSCT for the treatment of adults with thalassemia major and the role of this therapy has not yet been established for that indication.

For individuals with good-risk disease with an HLA-compatible sibling donor, the probability of disease-free survival (DFS) is 80–90%. In children who do not have liver disease and have received regular chelation therapy, the probability of survival with transfusion independence is over 90% (Holstein, 2011; La Nasa, 2005; Locatelli, 2005).

Worse results have been obtained in high-risk individuals where the probability of DFS is approximately 58% when transfusion independence after the allograft is achieved (La Nasa, 2005). Adults with thalassemia have more advanced disease and treatment-related organ complications, mainly because of prolonged exposure to iron overload. Adults generally have a worse outcome than children; their probabilities of overall survival (OS) and DFS are 65%–66% and 62%–65%, respectively (Smiers, 2010, Locatelli, 2005).

Data reported to the European Group for Blood and Marrow Transplantation hemoglobinopathy database (Shenoy et al, 2017) reflects two-year overall survival (OS) and event-free survival (EFS) rates of 88% and 81%, respectively, for individuals undergoing allogeneic HSCT for thalassemia. Among children < 2 years of age who received an HLA-identical sibling allograft, the OS and EFS rates at two years were 95% and 93%, respectively. Recipients > 18 years of age had OS and EFS rates of 80% and 76%, respectively.

Baronciani et al. (2016) published a retrospective non-interventional analysis of registry data involving 1493 consecutive patients with thalassemia major who underwent myeloablative allogeneic HSCT between 2000 and 2010. Data was derived from the European Group for Blood and Marrow Transplantation Hemoglobinopathy registry. Of the 1493 included transplants, 1359 (91%) were performed on patients <18 years old (median age 6.6, range 0.3–17); 133 (9%) were in patients aged 18 years or older (median age 22.9, range 18–45). Overall survival (OS) was 90–96% with an event-free survival (EFS) rate of 83–93% when transplant was performed before age 14 years. One hundred thirty-three (9%) transplants were in patients aged ≥18 years; median age 22.9 years (range 18-45). One thousand sixty-one (71.1%) HSCTs were performed using HLA-identical sibling donors, 127 (8.5%) from another HLA-matched relative, 57 (3.8%) from an unmatched relative and 210 (14.1%) from a matched unrelated donor. Data regarding HLA donor status was missing for 38 participants.

Two-year OS and EFS were 88% and 81, respectively, after a median observation period of two years with 250 patients having a documented follow-up 45 years. OS and EFS were 90%, 81% and 93% (p<0.001), and 82%, 76% and 85% (p = 0.003) in patients who had received bone marrow, peripheral blood or cord blood (alone or combined), respectively. A univariate analysis of the data for the 1060 patients who received a transplant from a matched sibling donor was performed to explore the impact of age on survival. Both OS and EFS significantly decreased with increasing age (P<0.001, test for trend). Limitations include retrospective study design.
Non-Myeloablative Allogeneic HSCT for Thalassemia: There is insufficient evidence in the published, peer-reviewed scientific literature regarding the feasibility of using non-myeloablative preparative regimens for patients with thalassemia. Data are limited to support the safety and effectiveness of this treatment. The ability to draw conclusions regarding improved health outcomes is limited by small patient populations, heterogeneous conditioning regimens, uncontrolled study design and short-term follow-up. Disease recurrence and graft-versus-host disease continue to be a source of morbidity and mortality following this therapy. Non-myeloablative regimens remain under clinical evaluation.

Literature Review
Resnick et al. (2007) reported the results of a cohort of 20 patients who underwent reduced toxicity fludarabine-based conditioning followed by allogeneic HSCT using matched-related and unrelated donors. Median patient age was 5.6 years. With a median follow-up of 39 months, 16 of 20 patients had sustained engraftment and were transfusion independent. The overall survival and thalassemia-free survival were 100% and 80%, respectively, at a median follow-up of 39 months. Larger cohorts of patients and prospective clinical trials are required to confirm the benefits of this approach as a possible better alternative to the existing protocols.

Contraindications to Transplantation
Many factors affect the outcome of tissue transplantation; 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 candidates. Relative contraindications to hematopoietic stem-cell transplantation (HSCT) include, but are not limited to:

- poor cardiac function (ejection fraction < 45%)
- poor liver function (bilirubin > 2.0mg/dl and transaminases greater than two times normal)
- poor renal function (creatinine clearance < 50ml/min)
- poor pulmonary function [diffusion capacity (DLCO) < 60% of predicted]
- presence of human immunodeficiency virus OR an active form of any ONE of the following:
  - hepatitis B virus (HBV)
  - hepatitis C virus (HCV)
  - human T-cell lymphotropic virus (HTLV)-1
- Karnofsky rating < 60% and/or Eastern Cooperative Oncology Group (ECOG) performance status > 2

Professional Societies/Organizations
National Marrow Donor Program (NMDP): The NMDP (1996-2017) lists hemoglobinopathies, including sickle cell disease (SCD) and thalassemia major, as diseases which are treatable by allogeneic hematopoietic stem-cell transplantation (HSCT). For SCD, referral for evaluation for stem-cell transplantation is recommended when the disease has an aggressive course (e.g., stroke, end-organ complications, frequent pain crises). For transfusion-dependent thalassemias, referral is recommended upon diagnosis of the disorder.

National Heart, Lung and Blood Institute (NHLBI): In an assessment titled “Evidence-Based Management of Sickle Cell Disease (2012), NHLBI notes stem-cell transplantation may offer a cure for a small number of people with sickle cell anemia. Although clinical trials have provided promising results, and cure appears to be possible in a large proportion of patients receiving HSCT, additional research is still needed that addresses the potential risks of this therapy (e.g., failure of engraftment and chronic graft-versus-host disease) before HSCT can become a widely used therapy.

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative (2014): No relevant statements.

Use Outside of the US:
European Society for Blood and Marrow Transplantation (EBMT) Inborn Error and EBMT Paediatric Working Parties (2014): On behalf of this professional society Angelucci et al. published indications and management recommendations for HSCT for thalassemia major and SCD. Regarding children and adolescents
with thalassemia major, the panel recommends young patients with an available HLA identical sibling should be offered HSCT as soon as possible before development of iron overload and iron-related tissue damage. Regarding adults, the panel recommends HSCT should be offered within controlled trials to adults who have been well-chelated since infancy. Regarding HSCT for SCD, the panel notes young patients with symptomatic SCD who have an HLA-matched sibling donor should be transplanted as early as possible, preferably at preschool age.

**Coding/Billing Information**

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when used to report myeloablative allogeneic bone marrow or blood-derived stem cell procedures for sickle cell disease or thalassemia major in children or young adults:**

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<th>CPT® Codes</th>
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<td>38205</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic</td>
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<td>38207</td>
<td>Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage</td>
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<td>38208</td>
<td>Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor</td>
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<td>Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion</td>
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<td>38212</td>
<td>Transplant preparation of hematopoietic progenitor cells; red blood cell removal</td>
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<td>38213</td>
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<td>38214</td>
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<td>38215</td>
<td>Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear, or buffy coat layer</td>
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<td>Cord blood-derived stem-cell transplantation, allogeneic</td>
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<td>S2150</td>
<td>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</td>
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**References**


