



MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Medical Policy

Allogeneic Hematopoietic Cell transplantation for Myelodysplastic Syndromes and Myeloproliferative Neoplasms

Table of Contents

- [Policy: Commercial](#)
- [Coding Information](#)
- [Information Pertaining to All Policies](#)
- [Policy: Medicare](#)
- [Description](#)
- [References](#)
- [Authorization Information](#)
- [Policy History](#)

Policy Number: 155

BCBSA Reference Number: 8.01.21

NCD/LCD: National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23)

Related Policies

- Placental and Umbilical Cord Blood as a Source of Stem Cells, [#285](#)
- Hematopoietic Cell Transplantation for Chronic Myelogenous Leukemia, [#212](#)
- Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia, [#150](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Myeloablative allogeneic hematopoietic cell transplantation (allo-HCT) may be **MEDICALLY NECESSARY** as a treatment of:

- Myelodysplastic syndromes **or**
- Myeloproliferative neoplasms.

Reduced-intensity conditioning allo-HCT may be **MEDICALLY NECESSARY** as a risk-adapted treatment of:

- Myelodysplastic syndromes **or**
- Myeloproliferative neoplasms in patients who are at high-risk of intolerance of a myeloablative conditioning regimen.

Myeloablative allo-HCT or reduced-intensity conditioning allo-HCT for myelodysplastic syndromes and myeloproliferative neoplasms that do not meet the criteria in the Policy Guidelines section is considered **INVESTIGATIONAL**.

The myeloid neoplasms are categorized according to criteria developed by the World Health Organization (WHO). They are risk-stratified according to the International Prognostic Scoring System (IPSS).

2008 WHO Classification Scheme for Myeloid Neoplasms

1. Acute myeloid leukemia
2. Myelodysplastic syndromes (MDS)
3. Myeloproliferative neoplasms (MPN)
 - 3.1 Chronic myelogenous leukemia
 - 3.2 Polycythemia vera
 - 3.3 Essential thrombocythemia
 - 3.4 Primary myelofibrosis
 - 3.5 Chronic neutrophilic leukemia
 - 3.6 Chronic eosinophilic leukemia, not otherwise categorized
 - 3.7 Hypereosinophilic leukemia
 - 3.8 Mast cell disease
 - 3.9 MPNs, unclassifiable
4. MDS/MPN
 - 4.1 Chronic myelomonocytic leukemia
 - 4.2 Juvenile myelomonocytic leukemia
 - 4.3 Atypical chronic myeloid leukemia
 - 4.4 MDS/MPN, unclassifiable
5. Myeloid neoplasms associated with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB*, or *FGFR1*
 - 5.1 Myeloid neoplasms associate with *PDGFRA* rearrangement
 - 5.2 Myeloid neoplasms associate with *PDGFRB* rearrangement
 - 5.3 Myeloid neoplasms associate with *FGFR1* rearrangement (8p11 myeloproliferative syndrome)

2008 WHO Classification of MDS

1. Refractory anemia (RA)
2. RA with ring sideroblasts (RARS)
3. Refractory cytopenia with multilineage dysplasia (RCMD)
4. RCMD with ring sideroblasts
5. RA with excess blasts 1 and 2 (RAEB 1 and 2)
6. del 5q syndrome
7. unclassified MDS

Risk Stratification of MDS

Risk stratification for MDS is performed using the IPSS (see Table PG1). This system was developed after pooling data from 7 studies that used independent, risk-based prognostic factors. The prognostic model and the scoring system were built based on blast count, degree of cytopenia, and blast percentage. Risk scores were weighted relative to their statistical power. This system is widely used to divide patients into 2 categories: (1) low-risk and (2) high-risk groups (see Table PG2). The low-risk group includes low-risk and Int-1 IPSS groups; the goals in low-risk MDS patients are to improve quality of life and achieve transfusion independence. In the high-risk group—which includes intermediate-2 and high risk IPSS groups—the goals are slowing the progression of disease to acute myeloid leukemia (AML) and improving survival. IPSS is usually calculated on diagnosis. The role of lactate dehydrogenase, marrow fibrosis, and β 2-microglobulin also should be considered after establishing IPSS. If elevated, the prognostic category becomes worse by 1 category change.

Table PG1. International Prognostic Scoring System: Myelodysplastic Syndrome Prognostic Variables

Variable	0	0.5	1.0	1.5	2.0
Marrow blasts, %	<5%	5%-10%	-	11%-20%	21%-30%
Karyotype	Good	Intermediate	Poor		
Cytopenias	0/1	2/3	-	-	-

Table PG2. International Prognostic Scoring System: Myelodysplastic Syndrome Clinical Outcomes

Risk Group	Total Score	Median Survival, y	Time for 25% to Progress to AML
------------	-------------	--------------------	---------------------------------

Low	0	5.7	9.4
intermediate-1	0.5-1.0	3.5	3.3
intermediate-2	1.5-2.0	1.2	1.12
High	≥2.5	0.4	0.2

AML: acute myelocytic leukemia.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

Allogeneic HSCT for myelofibrosis (MF)

Effective for claims with dates of service on or after January 27, 2016, allogeneic HSCT for myelofibrosis (MF) is covered by Medicare only for beneficiaries with Dynamic International Prognostic Scoring System (DIPSSplus) intermediate-2 or High primary or secondary MF and participating in an approved prospective clinical study.

All Medicare approved studies must use appropriate statistical techniques in the analysis to control for selection bias and potential confounding by age, duration of diagnosis, disease classification, DIPSSplus score, comorbid conditions, type of preparative/conditioning regimen, graft vs. host disease (GVHD) prophylaxis, donor type and cell source.

A prospective clinical study seeking Medicare coverage for allogeneic HSCT for myelofibrosis pursuant to Coverage with Evidence Development (CED) must address the following question:

Compared to patients who do not receive allogeneic HSCT, do Medicare beneficiaries with MF who receive allogeneic HSCT transplantation have improved outcomes as indicated by:

- Graft vs. host disease (acute and chronic);
- Other transplant-related adverse events;
- Overall survival; and
- (optional) Quality of life?

All CMS-approved clinical studies and registries must adhere to the below listed standards of scientific integrity and relevance to the Medicare population:

All CMS-approved clinical studies and registries must adhere to the below listed standards of scientific integrity and relevance to the Medicare population:

- a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
- b. The rationale for the study is well supported by available scientific and medical evidence.
- c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
- d. The study design is methodologically appropriate, and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
- e. The study is sponsored by an organization or individual capable of completing it successfully.
- f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
- g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
- h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
- i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is

life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.

- j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Quality (AHRQ) Registry of Patient Registries (RoPR).
- k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessible manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
- l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
- m. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Facilities must submit the required transplant essential data to the Stem Cell Therapeutics Outcomes Database.

Medical necessity criteria and coding guidance can be found through the link below.

[National Coverage Determinations \(NCDs\)](#)

National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23)

Note: To review the specific NCD, please remember to click "accept" on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .
Medicare HMO BlueSM	Prior authorization is required .
Medicare PPO BlueSM	Prior authorization is required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above **medical necessity criteria MUST** be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic

HCPCS Codes

HCPCS codes:	Code Description
S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)

ICD-10 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
30233G1	Transfusion of Nonautologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X1	Transfusion of Nonautologous Cord Blood Stem Cells into Peripheral Vein, Percutaneous Approach
30233Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Peripheral Vein, Percutaneous Approach
30243G1	Transfusion of Nonautologous Bone Marrow into Central Vein, Percutaneous Approach
30243X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Vein, Percutaneous Approach
30243Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Vein, Percutaneous Approach
30263G1	Transfusion of Nonautologous Bone Marrow into Central Artery, Percutaneous Approach
30263X1	Transfusion of Nonautologous Cord Blood Stem Cells into Central Artery, Percutaneous Approach
30263Y1	Transfusion of Nonautologous Hematopoietic Stem Cells into Central Artery, Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

Description

Myelodysplastic Syndromes

MDS can occur as a primary (idiopathic) disease or can be secondary to cytotoxic therapy, ionizing radiation, or other environmental insults. Chromosomal abnormalities are seen in 40% to 60% of patients, frequently involving deletions of chromosome 5 or 7 or an extra chromosome as in trisomy 8. Most MDS

diagnoses occur in individuals older than age 55 to 60 years, with an age-adjusted incidence of 62% among individuals older than age 70 years. Patients succumb either to disease progression to acute myeloid leukemia (AML) or to complications of pancytopenias. Patients with higher blast counts or complex cytogenetic abnormalities have a greater likelihood of progressing to AML than do other patients.

MDS Classification and Prognosis

The French-American-British system was used to classify MDS into 5 subtypes: (1) refractory anemia; (2) refractory anemia with ringed sideroblasts; (3) refractory anemia with excess blasts; (4) refractory anemia with excess blasts in transformation; and (5) chronic myelomonocytic leukemia. The French-American-British system was supplanted by that of the World Health Organization (WHO), which records the number of lineages in which dysplasia is seen (unilineage vs. multilineage), separates the 5q-syndrome, and reduces the threshold maximum blast percentage for the diagnosis of MDS from 30% to 20%.

The most commonly used prognostic scoring system for MDS is the International Prognostic Scoring System (IPSS), which groups patients into 1 of 4 prognostic categories based on the number of cytopenias, cytogenetic profile, and the percentage of blasts in the bone marrow. This system underweights the clinical importance of severe, life-threatening neutropenia and thrombocytopenia in therapeutic decisions and does not account for the rate of change in critical parameters (eg, peripheral blood counts, blast percentage). However, the IPSS has been useful in a comparative analysis of clinical trial results and its utility confirmed at many institutions. An updated 5-category IPSS has been proposed for prognosis in patients with primary MDS or secondary AML to account for chromosomal abnormalities frequently seen in MDS.¹ This system stratifies patients into 5 categories: very poor, poor, intermediate, good, and very good. There has been an investigation into using the 5-category IPSS to better characterize risk in MDS. A second prognostic scoring system incorporates the WHO subgroup classification that accounts for blast percentage, cytogenetics, and severity of cytopenias as assessed by transfusion requirements. The WHO classification-based Prognostic Scoring System uses a 6-category system, which allows more precise prognostication of overall survival (OS) duration, as well as risk for progression to AML. This system is not yet in widespread use in clinical trials.

MDS Treatment

Treatment of nonprogressing MDS has involved best supportive care, including red blood cell and platelet transfusions and antibiotics. Active therapy was given only when MDS progressed to AML or resembled AML with severe cytopenias. An array of therapies are now available to treat MDS, including hematopoietic growth factors (eg, erythropoietin, darbepoetin, granulocyte colony-stimulating factor), transcriptional-modifying therapy (eg, FDA-approved hypomethylating agents, nonapproved histone deacetylase inhibitors), immunomodulators (eg, lenalidomide, thalidomide, antithymocyte globulin, cyclosporine A), low-dose chemotherapy (eg, cytarabine), and allogeneic hematopoietic cell transplantation (allo-HCT). Given the spectrum of treatments available, the goal of therapy must be decided upfront whether it is to improve anemia, thrombocytopenia, or neutropenia, to eliminate the need for red blood cell transfusion, to achieve complete remission, or to cure the disease.

Allo-HCT is the only approach with curative potential, but its use is governed by patient age, performance status, medical comorbidities, the patient's risk preference, and severity of MDS at presentation. Allo-HCT is discussed in more detail in a subsequent section.

Chronic Myeloproliferative Neoplasms

Chronic MPN are clonal bone marrow stem cell disorders; as a group, approximately 8400 MPN are diagnosed annually in the United States. Like MDS, MPN primarily occurs in older individuals, with approximately 67% reported in patients aged 60 years and older.

MPN are characterized by the slow but progressive expansion of a clone of cells with the potential evolution into a blast crisis similar to AML. MPN share a common stem cell derived clonal heritage, with phenotypic diversity attributed to abnormal variations in signal transduction as the result of a spectrum of variants that affects protein tyrosine kinases or related molecules. The unifying characteristic common to all MPN is effective clonal myeloproliferation resulting in peripheral granulocytosis, thrombocytosis, or erythrocytosis that is devoid of dyserythropoiesis, granulocytic dysplasia, or monocytosis.

MPN Classification

The WHO (2008) classification scheme replaced the term chronic *myeloproliferative disorder* with the term *myeloproliferative neoplasm*. MPN are a subdivision of myeloid neoplasms that includes 4 classic disorders: chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, and primary myelofibrosis. The WHO classification also includes chronic neutrophilic leukemia, chronic eosinophilic leukemia/hypereosinophilic syndrome, mast cell disease, and MPN unclassifiable.

MPN Treatment

In indolent, nonprogressing cases, therapeutic approaches are based on relief of symptoms. Supportive therapy may include prevention of thromboembolic events. Hydroxyurea may be used in cases of high-risk essential thrombocythemia and polycythemia vera, and intermediate- and high-risk primary myelofibrosis.

The FDA (2011) approved the orally administered selective Janus kinase 1 and 2 inhibitor ruxolitinib for the treatment of intermediate- or high-risk myelofibrosis. Ruxolitinib has been associated with improved OS, spleen size, and symptoms of myelofibrosis compared with placebo.² The Randomized Study of Ruxolitinib Tablets Compared to Best Available Therapy in Subjects With Primary Myelofibrosis, Post-Polycythemia Vera-Myelofibrosis or Post-Essential Thrombocythemia Myelofibrosis (COMFORT-II trial [2013]) compared ruxolitinib with best available therapy in patients who had intermediate- and high-risk myelofibrosis, and demonstrated improvements in spleen volume and OS.³ In a randomized trial comparing ruxolitinib with best available therapy (including antineoplastic agents, most commonly hydroxyurea, glucocorticoids) with no therapy for treatment of myelofibrosis, Harrison et al (2012) reported improvements in spleen size and quality of life, but not OS.⁴

Myeloablative allo-HCT has been considered the only potentially curative therapy, but because most patients are of advanced age with attendant comorbidities, its use is limited to those who can tolerate the often-severe treatment-related adverse events of this procedure. However, the use of reduced-intensity conditioning (RIC) of conditioning regimens for allo-HCT has extended the potential benefits of this procedure to selected individuals with these disorders. Allo-HCT is discussed in more detail in the next section.

Hematopoietic Cell Transplantation

HCT is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allo-HCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

Conditioning for Hematopoietic Cell Transplantation

Conventional Conditioning

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (eg, cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs.

Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease, which increases susceptibility to opportunistic infections.

The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not graft-versus-host disease.

Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation

RIC refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism. In this review, the term *reduced-intensity conditioning* will refer to all conditioning regimens intended to be nonmyeloablative.

Summary

Myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN) refer to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic leukemia. Allogeneic hematopoietic cell transplantation (HCT) has been proposed as a curative treatment option for patients with these disorders.

For individuals who have MDS or MPN who receive myeloablative conditioning allogeneic HCT, the evidence includes case series, which are often heterogeneous in terms of diseases included. Relevant outcomes are overall survival (OS), disease-specific survival, and treatment-related mortality and morbidity. Primarily uncontrolled, observational studies of HCT for MDS have reported a relatively large range of overall and progression-free survival rates, which reflect the heterogeneity in patient populations, conditioning regimens, and other factors. Reported estimates for 3- to 5-year OS of 40% to 50% are typical. For HCT for MPN, data are more limited. At least 1 comparative study of HCT for myelofibrosis has demonstrated improved survival using HCT compared with standard therapy. At present, HCT is the only potentially curative treatment option for patients with MDS and MPN. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have MDS or MPN who receive reduced-intensity conditioning allogeneic HCT, the evidence includes RCTs and retrospective observational series. Relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. Evidence from RCT trials and retrospective, nonrandomized comparisons have suggested that reduced-intensity conditioning may be used as a risk-adapted strategy in high-risk patients who are older and have more comorbidities without significantly worsening OS. Reduced-intensity conditioning appears to be associated with lower rates of nonrelapse mortality but higher cancer relapse than myeloablative HCT. At present, HCT is the only potentially curative treatment option for patients with MDS and MPN. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Policy History

Date	Action
6/2020	BCBSA National medical policy review. Policy statement for RIC allo-HCT changed to specify it as a risk-adapted strategy for patients at high-risk of MAC intolerance, which

	is meant to encompass both older age and medical co-occurring conditions. Effective 6/1/2020.
4/2020	Bone marrow harvesting codes were removed. Outpatient prior authorization is not required.
3/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
1/2019	Outpatient prior authorization is required for all commercial products including Medicare Advantage. Effective 1/1/2019.
2/2018	New references added from BCBSA National medical policy.
2/2018	Clarified coding information.
5/2017	New references added from BCBSA National medical policy.
6/2017	New references added from BCBSA National medical policy.
3/2017	BCBSA National medical policy review. Title changed. New references added.
12/2016	Coverage clarified for Medicare Advantage based on National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23). 12/14/2016
3/2016	New references added from BCBSA National medical policy.
9/2015	Clarified coding language.
12/2014	New references added from BCBSA National medical policy.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
2/2014	New references added from BCBSA National medical policy.
12/2012	Updated to add new CPT code 38243.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group – Hematology and Oncology. No changes to policy statements.
1/1/2010	Medical policy 155 effective 1/1/2010 describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

References

1. Schanz J, Tuchler H, Sole F, et al. New comprehensive cytogenetic scoring system for primary myelodysplastic syndromes (MDS) and oligoblastic acute myeloid leukemia after MDS derived from an international database merge. *J Clin Oncol*. Mar 10 2012;30(8):820-829. PMID 22331955
2. Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med*. Mar 1 2012;366(9):799-807. PMID 22375971
3. Cervantes F, Vannucchi AM, Kiladjan JJ, et al. Three-year efficacy, safety, and survival findings from COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for myelofibrosis. *Blood*. Dec 12 2013;122(25):4047-4053. PMID 24174625
4. Harrison C, Kiladjan JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med*. Mar 01 2012;366(9):787-798. PMID 22375970
5. Kasner MT, Luger SM. Update on the therapy for myelodysplastic syndrome. *Am J Hematol*. Mar 2009;84(3):177-186. PMID 19195035
6. Kindwall-Keller T, Isola LM. The evolution of hematopoietic SCT in myelodysplastic syndrome. *Bone Marrow Transplant*. Apr 2009;43(8):597-609. PMID 19252532
7. Oliansky DM, Antin JH, Bennett JM, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of myelodysplastic syndromes: an evidence-based review. *Biol Blood Marrow Transplant*. Feb 2009;15(2):137-172. PMID 19167676

8. Koenecke C, Gohring G, de Wreede LC, et al. Impact of the revised International Prognostic Scoring System, cytogenetics and monosomal karyotype on outcome after allogeneic stem cell transplantation for myelodysplastic syndromes and secondary acute myeloid leukemia evolving from myelodysplastic syndromes: a retrospective multicenter study of the European Society of Blood and Marrow Transplantation. *Haematologica*. Mar 2015;100(3):400-408. PMID 25552702
9. Beelen DW, Trenschele R, Steljes M, et al. Treosulfan or busulfan plus fludarabine as conditioning treatment before allogeneic haemopoietic stem cell transplantation for older patients with acute myeloid leukaemia or myelodysplastic syndrome (MC-FludT.14/L): a randomised, non-inferiority, phase 3 trial. *Lancet Haematol*, 2019 Oct 14. PMID 31606445
10. Scott BL, Pasquini MC, Logan BR et al. Myeloablative Versus Reduced-Intensity Hematopoietic Cell Transplantation for Acute Myeloid Leukemia and Myelodysplastic Syndromes. *J. Clin. Oncol.*, 2017 Apr 6;35(11). PMID 28380315
11. Kroger N, Iacobelli S, Franke GN, et al. Dose-Reduced Versus Standard Conditioning Followed by Allogeneic Stem-Cell Transplantation for Patients With Myelodysplastic Syndrome: A Prospective Randomized Phase III Study of the EBMT (RICMAC Trial). *J. Clin. Oncol.*, 2017 May 4;35(19). PMID 28463633
12. Akhtari M. When to treat myelodysplastic syndromes. *Oncology (Williston Park)*. May 2011;25(6):480-486. PMID 21717901
13. Deeg HJ, Sandmaier BM. Who is fit for allogeneic transplantation? *Blood*. Dec 2 2010;116(23):4762-4770. PMID 20702782
14. Giralt SA, Horowitz M, Weisdorf D, et al. Review of stem-cell transplantation for myelodysplastic syndromes in older patients in the context of the Decision Memo for Allogeneic Hematopoietic Stem Cell Transplantation for Myelodysplastic Syndrome emanating from the Centers for Medicare and Medicaid Services. *J Clin Oncol*. Feb 10 2011;29(5):566-572. PMID 21220586
15. Deeg HJ, Bartenstein M. Allogeneic hematopoietic cell transplantation for myelodysplastic syndrome: current status. *Arch Immunol Ther Exp (Warsz)*. Feb 2012;60(1):31-41. PMID 22143157
16. Garcia-Manero G. Myelodysplastic syndromes: 2012 update on diagnosis, risk-stratification, and management. *Am J Hematol*. Jul 2012;87(7):692-701. PMID 22696212
17. Kroger N. Allogeneic stem cell transplantation for elderly patients with myelodysplastic syndrome. *Blood*. Jun 14 2012;119(24):5632-5639. PMID 22504927
18. Barrett AJ, Savani BN. Allogeneic stem cell transplantation for myelodysplastic syndrome. *Semin Hematol*. Jan 2008;45(1):49-59. PMID 18179969
19. Blaise D, Vey N, Faucher C, et al. Current status of reduced-intensity-conditioning allogeneic stem cell transplantation for acute myeloid leukemia. *Haematologica*. Apr 2007;92(4):533-541. PMID 17488664
20. Deschler B, de Witte T, Mertelsmann R, et al. Treatment decision-making for older patients with high-risk myelodysplastic syndrome or acute myeloid leukemia: problems and approaches. *Haematologica*. Nov 2006;91(11):1513-1522. PMID 17082009
21. Huisman C, Meijer E, Petersen EJ, et al. Hematopoietic stem cell transplantation after reduced intensity conditioning in acute myelogenous leukemia patients older than 40 years. *Biol Blood Marrow Transplant*. Feb 2008;14(2):181-186. PMID 18215778
22. Kroger N, Bornhauser M, Ehninger G, et al. Allogeneic stem cell transplantation after a fludarabine/busulfan- based reduced-intensity conditioning in patients with myelodysplastic syndrome or secondary acute myeloid leukemia. *Ann Hematol*. Jun 2003;82(6):336-342. PMID 12728337
23. Laport GG, Sandmaier BM, Storer BE, et al. Reduced-intensity conditioning followed by allogeneic hematopoietic cell transplantation for adult patients with myelodysplastic syndrome and myeloproliferative disorders. *Biol Blood Marrow Transplant*. Feb 2008;14(2):246-255. PMID 18215785
24. Martino R, Caballero MD, Perez-Simon JA, et al. Evidence for a graft-versus-leukemia effect after allogeneic peripheral blood stem cell transplantation with reduced-intensity conditioning in acute myelogenous leukemia and myelodysplastic syndromes. *Blood*. Sep 15 2002;100(6):2243-2245. PMID 12200391
25. Mesa RA. Navigating the evolving paradigms in the diagnosis and treatment of myeloproliferative disorders. *Hematology Am Soc Hematol Educ Program*. Nov 2007:355-362. PMID 18024651
26. Tauro S, Craddock C, Peggs K, et al. Allogeneic stem-cell transplantation using a reduced-intensity conditioning regimen has the capacity to produce durable remissions and long-term disease-free

- survival in patients with high-risk acute myeloid leukemia and myelodysplasia. *J Clin Oncol.* Dec 20 2005;23(36):9387-9393. PMID 16314618
27. Valcarcel D, Martino R. Reduced-intensity conditioning for allogeneic hematopoietic stem cell transplantation in myelodysplastic syndromes and acute myelogenous leukemia. *Curr Opin Oncol.* Nov 2007;19(6):660-666. PMID 17906468
 28. Valcarcel D, Martino R, Caballero D, et al. Sustained remissions of high-risk acute myeloid leukemia and myelodysplastic syndrome after reduced-intensity conditioning allogeneic hematopoietic transplantation: chronic graft-versus-host disease is the strongest factor improving survival. *J Clin Oncol.* Feb 01 2008;26(4):577-584. PMID 18086801
 29. Zeng W, Huang L, Meng F, et al. Reduced-intensity and myeloablative conditioning allogeneic hematopoietic stem cell transplantation in patients with acute myeloid leukemia and myelodysplastic syndrome: a meta-analysis and systematic review. *Int J Clin Exp Med.* Jan 2014;7(11):4357-4368. PMID 25550955
 30. Aoki K, Ishikawa T, Ishiyama K, et al. Allogeneic haematopoietic cell transplantation with reduced-intensity conditioning for elderly patients with advanced myelodysplastic syndromes: a nationwide study. *Br J Haematol.* Feb 2015;168(3):463-466. PMID 25228239
 31. Kim H, Lee JH, Joo YD, et al. A randomized comparison of cyclophosphamide vs. reduced dose cyclophosphamide plus fludarabine for allogeneic hematopoietic cell transplantation in patients with aplastic anemia and hypoplastic myelodysplastic syndrome. *Ann Hematol.* Sep 2012;91(9):1459-1469. PMID 22526363
 32. Basquiera AL, Pizzi S, Correas AG, et al. Allogeneic hematopoietic stem cell transplantation in pediatric myelodysplastic syndromes: a multicenter experience from Argentina. *Pediatr Blood Cancer.* Jan 2015;62(1):153-157. PMID 25264233
 33. Boehm A, Sperr WR, Kalhs P, et al. Long-term follow-up after allogeneic stem cell transplantation in patients with myelodysplastic syndromes or secondary acute myeloid leukemia: a single-center experience. *Wien Klin Wochenschr.* Jan 2014;126(1-2):23-29. PMID 24249320
 34. Damaj G, Mohty M, Robin M, et al. Upfront allogeneic stem cell transplantation after reduced-intensity/nonmyeloablative conditioning for patients with myelodysplastic syndrome: a study by the Societe Francaise de Greffe de Moelle et de Therapie Cellulaire. *Biol Blood Marrow Transplant.* Sep 2014;20(9):1349-1355. PMID 24838178
 35. Di Stasi A, Milton DR, Poon LM, et al. Similar transplantation outcomes for acute myeloid leukemia and myelodysplastic syndrome patients with haploidentical versus 10/10 human leukocyte antigen-matched unrelated and related donors. *Biol Blood Marrow Transplant.* Dec 2014;20(12):1975-1981. PMID 25263628
 36. Onida F, Brand R, van Biezen A, et al. Impact of the International Prognostic Scoring System cytogenetic risk groups on the outcome of patients with primary myelodysplastic syndromes undergoing allogeneic stem cell Neoplasms transplantation from human leukocyte antigen-identical siblings: a retrospective analysis of the European Society for Blood and Marrow Transplantation-Chronic Malignancies Working Party. *Haematologica.* Oct 2014;99(10):1582-1590. PMID 25085359
 37. Oran B, Kongtim P, Popat U, et al. Cytogenetics, donor type, and use of hypomethylating agents in myelodysplastic syndrome with allogeneic stem cell transplantation. *Biol Blood Marrow Transplant.* Oct 2014;20(10):1618-1625. PMID 24953017
 38. Yoshimi A, Strahm B, Baumann I, et al. Hematopoietic stem cell transplantation in children and young adults with secondary myelodysplastic syndrome and acute myelogenous leukemia after aplastic anemia. *Biol Blood Marrow Transplant.* Mar 2014;20(3):425-429. PMID 24316460
 39. Basquiera AL, Rivas MM, Remaggi G, et al. Allogeneic hematopoietic stem cell transplantation in adults with myelodysplastic syndrome: Experience of the Argentinean Group of Bone Marrow Transplantation (GATMO). *Hematology.* Apr 2016;21(3):162-169. PMID 26147089
 40. Symeonidis A, van Biezen A, de Wreede L, et al. Achievement of complete remission predicts outcome of allogeneic haematopoietic stem cell transplantation in patients with chronic myelomonocytic leukaemia. A study of the Chronic Malignancies Working Party of the European Group for Blood and Marrow Transplantation. *Br J Haematol.* Jul 26 2015;171(2):239-246. PMID 26212516
 41. Pohlen M, Groth C, Sauer T, et al. Outcome of allogeneic stem cell transplantation for AML and myelodysplastic syndrome in elderly patients (60 years). *Bone Marrow Transplant.* Nov 2016;51(11):1441-1448. PMID 27295269

42. Heidenreich S, Ziagkos D, de Wreede LC, et al. Allogeneic stem cell transplantation for patients age \geq 70 years with myelodysplastic syndrome: a retrospective study of the MDS Subcommittee of the Chronic Malignancies Working Party of the EBMT. *Biol Blood Marrow Transplant*. Jan 2017;23(1):44-52. PMID 27720995
43. Tefferi A, Vainchenker W. Myeloproliferative neoplasms: molecular pathophysiology, essential clinical understanding, and treatment strategies. *J Clin Oncol*. Feb 10 2011;29(5):573-582. PMID 21220604
44. McLornan DP, Mead AJ, Jackson G, et al. Allogeneic stem cell transplantation for myelofibrosis in 2012. *Br J Haematol*. May 2012;157(4):413-425. PMID 22463701
45. Ballen KK, Shrestha S, Sobocinski KA, et al. Outcome of transplantation for myelofibrosis. *Biol Blood Marrow Transplant*. Mar 2010;16(3):358-367. PMID 19879949
46. Gupta V, Malone AK, Hari PN, et al. Reduced-intensity hematopoietic cell transplantation for patients with primary myelofibrosis: a cohort analysis from the center for international blood and marrow transplant research. *Biol Blood Marrow Transplant*. Jan 2014;20(1):89-97. PMID 24161923
47. Kroger N, Giorgino T, Scott BL, et al. Impact of allogeneic stem cell transplantation on survival of patients less than 65 years of age with primary myelofibrosis. *Blood*. May 21 2015;125(21):3347-3350; quiz 3364. PMID 25784679
48. Kroger N, Holler E, Kobbe G, et al. Allogeneic stem cell transplantation after reduced-intensity conditioning in patients with myelofibrosis: a prospective, multicenter study of the Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation. *Blood*. Dec 17 2009;114(26):5264-5270. PMID 19812383
49. Gupta V, Kroger N, Aschan J, et al. A retrospective comparison of conventional intensity conditioning and reduced-intensity conditioning for allogeneic hematopoietic cell transplantation in myelofibrosis. *Bone Marrow Transplant*. Sep 2009;44(5):317-320. PMID 19234505
50. Abellsson J, Merup M, Birgegard G, et al. The outcome of allo-HSCT for 92 patients with myelofibrosis in the Nordic countries. *Bone Marrow Transplant*. Mar 2012;47(3):380-386. PMID 21552298
51. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes, Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed December 3, 2019.
52. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms, Version 3.2019. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed December 4, 2019.
53. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant*. Nov 2015;21(11):1863-1869. PMID 26256941
54. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation Formerly 110.8.1 (110.23). 2016; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366> Accessed December 4, 2019.