

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

<b>CLINICAL BENEFIT</b>	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
<b>Effective Date:</b>	<b>4/1/2025</b>

[POLICY RATIONALE](#)  
[DISCLAIMER](#)  
[POLICY HISTORY](#)

[PRODUCT VARIATIONS](#)  
[DEFINITIONS](#)  
[CODING INFORMATION](#)

[DESCRIPTION/BACKGROUND](#)  
[BENEFIT VARIATIONS](#)  
[REFERENCES](#)

### I. POLICY

Myeloablative allogeneic hematopoietic cell transplantation (allo-HCT) may be considered **medically necessary** as a treatment of

- myelodysplastic syndromes (see Policy Guidelines); **or**
- myeloproliferative neoplasms (see Policy Guidelines).

Reduced-intensity conditioning (RIC) allo-HCT may be considered **medically necessary** for individuals who meet the policy guidelines for the medical conditions listed above and who are at high-risk for not being able to tolerate a conventional myeloablative conditioning regimen (see Policy Guidelines).

Myeloablative allo-HCT or reduced-intensity conditioning allo-HCT for myelodysplastic syndromes and myeloproliferative neoplasms that does not meet the criteria in the Policy Guidelines is considered **investigational**. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

### Policy Guidelines

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

### 2022 WHO Classification Scheme for Myeloid Neoplasms and Histiocytic/Dendritic Neoplasms

#### Clonal hematopoiesis (CH)

- CH of indeterminate potential (CHIP)
- Clonal cytopenia of undetermined significance (CCUS)

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

### Myeloproliferative neoplasms (MPN)

- Chronic myeloid leukemia (CML), BCR-ABL1<sup>+</sup>
- Chronic neutrophilic leukemia (CNL)
- Polycythemia vera
- Primary myelofibrosis (PMF)
- Essential thrombocythemia
- Chronic eosinophilic leukemia
- MPN, not otherwise specified
- Juvenile myelomonocytic leukemia

### Mastocytosis

- Cutaneous mastocytosis
- Systemic mastocytosis
- Mast cell sarcoma

### Childhood MDS

- Childhood MDS with low blasts
  - Hypocellular
  - Not otherwise specified
- Childhood MDS with increased blasts

### Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK)

### Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)

- Chronic myelomonocytic leukemia (CMML)
- MDS/MPN with neutrophilia
- MDS/MPN with SF3B1 mutation and thrombocytosis
- MDS/MPN, not otherwise specified

### Myelodysplastic neoplasms (MDS)

- MDS with defining genetic abnormalities
  - MDS with low blasts and isolated 5q deletion (MDS-5q)
  - MDS with low blasts and SF3B1 mutation (MDS-SF3B1), or MDS with low blasts and ring sideroblasts
  - MDS with biallelic TP53 inactivation (MDS-biTP53)
- MDS, morphologically defined
  - MDS with low blasts (MDS-LB)
  - MDS, hypoplastic (MDS-h)
  - MDS with increased blasts (MDS-IB)
    - MDS-IB1
    - MDS-IB2
    - MDS with fibrosis (MDS-f)

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

### Acute myeloid leukemia (AML)

- AML with defining genetic abnormalities
- AML, defined by differentiation

### Secondary myeloid neoplasms

- Myeloid neoplasms post cytotoxic therapy
- Myeloid neoplasms associated with germline predisposition

### Dendritic cell and histiocytic neoplasms

- Plasmacytoid dendritic cell neoplasms
- Langerhans cell and other dendritic cell neoplasms
- Histiocytic neoplasms

### Acute leukemias of ambiguous lineage (ALAL)

- ALAL with defining genetic abnormalities
- ALAL, immunophenotypically defined

### Genetic tumor syndromes with predisposition to myeloid neoplasia

### 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 group individuals into either low-risk and or high-risk groups (see Table PG2). The low-risk group includes low-risk and Intermediate-1 IPSS groups; treatment goals in low-risk MDS individuals are to improve quality of life and achieve transfusion independence. In the high-risk group which includes intermediate-2 and high-risk IPSS groups, treatment goals are slowing disease progression to AML and improving survival. IPSS is usually calculated on diagnosis. The role of lactate dehydrogenase, marrow fibrosis, and  $\beta_2$ -microglobulin also should be considered after establishing IPSS. If elevated, the prognostic category becomes worse by one category change.

**Table PG1. IPSS: Myelodysplastic Syndrome Prognostic Variables**

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

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

**Table PG2. IPSS: Myelodysplastic Syndrome Clinical Outcomes**

<b>Risk Group</b>	<b>Total Score</b>	<b>Median Survival, y</b>	<b>Time for 25% of individuals to Progress to AML</b>
<b>Low</b>	0	5.7	9.4 years
<b>Intermediate-1</b>	0.5-1.0	3.5	3.3 years
<b>Intermediate-2</b>	1.5-2.0	1.2	1.12 years
<b>High</b>	≥2.5	0.4	0.2 years

AML: acute myelocytic leukemia; IPSS: International Prognostic Scoring System.

An updated 5-category IPSS has been proposed for prognosis in individuals with primary MDS or secondary AML to account for chromosomal abnormalities frequently seen in MDS (Schanz et al, 2012). This system stratifies individuals into five categories: very poor, poor, intermediate, good, and very good. There has been investigation into using the 5-category IPSS to better characterize risk in MDS.

Given the long natural history of MDS, allogeneic hematopoietic stem cell transplantation (allo-HCT) is typically considered in individuals with increasing numbers of blasts, signaling a possible transformation to AML. Subtypes falling into this category include refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, or chronic myelomonocytic leukemia (CMML).

Individuals with refractory anemia with or without ringed sideroblasts may be considered candidates for allo-HCT when chromosomal abnormalities are present or the disorder is associated with the development of significant cytopenias (e.g., neutrophils <500/mm<sup>3</sup>, platelets <20,000/mm<sup>3</sup>).

Individuals with myeloproliferative neoplasms (MPN) may be considered candidates for allo-HCT when there is progression to myelofibrosis toward acute leukemia. In addition, allo-HCT may be considered in individuals with essential thrombocythemia with an associated thrombotic or hemorrhagic disorder. Use of allo-HCT should be based on the following criteria: cytopenias, transfusion dependence, increasing blast percentage over 5%, and age.

Some individuals for whom a conventional myeloablative allo-HCT could be curative may be candidates for reduced-intensity conditioning (RIC) allo-HCT. These include those individuals whose age (typically >60 years) or comorbidities (e.g., liver or kidney dysfunction, generalized debilitation, prior intensive chemotherapy, low Karnofsky Performance Status) preclude use of a standard myeloablative conditioning (MAC) regimen. The ideal allogeneic donors are human leukocyte antigen (HLA) –identical siblings, matched at the HLA-A, -B, and -DR loci (6/6). Related donors mismatched at one locus are also considered suitable donors. A matched, unrelated donor identified through the National Marrow Donor Registry is typically the next option considered. Recently, there has been interest in haploidentical donors, typically a parent or a child of the individual, who usually share only three of the six major histocompatibility

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

antigens. Most individuals will have such a donor; however, the risk of graft-versus-host disease (GVHD) and overall morbidity of the procedure may be severe, and experience with these donors is not as GVHD extensive as that with matched donors.

Evidence and clinical guidelines suggest RIC allo-HCT may be considered as a risk-adapted strategy for high-risk individuals of MAC-intolerance as follows:

### MDS

- Older age
- IPSS intermediate-2 or high risk
- Multiple comorbidities (e.g., hematopoietic cell transplantation -comorbidity index (HCT-CI) score higher than 2)
- Red blood cell transfusion dependence
- Neutropenia
- Thrombocytopenia
- High-risk cytogenetics
- Increasing blast percentage

### Myeloproliferative neoplasm

- Cytopenias
- Transfusion dependence
- Increasing blast percentage over 5%
- Age 60 to 65 years

### ***Cross-References:***

**MP 9.040 Hematopoietic Cell Transplantation for Acute Myeloid Leukemia**

**MP 9.039 Hematopoietic Cell Transplantation for Chronic Myeloid Leukemia**

## II. PRODUCT VARIATIONS

[Top](#)

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

**FEP PPO:** Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at <https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

## III. DESCRIPTION/BACKGROUND

[Top](#)

Myelodysplastic syndromes (MDS) and myeloproliferative neoplasms refer to a heterogeneous group of clonal hematopoietic disorders with the potential to transform into acute myelocytic

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

leukemia. Allogeneic hematopoietic cell transplantation (allo-HCT) has been proposed as a curative treatment option for individuals with these disorders.

### MYELOYDYSPLASTIC SYNDROMES

Myelodysplastic syndrome (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 individuals, 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. Individuals succumb either to disease progression to acute myeloid leukemia (AML) or to complications of pancytopenias. Individuals with higher blast counts or complex cytogenetic abnormalities have a greater likelihood of progressing to AML than do other individuals.

#### Myelodysplastic Syndrome 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 differentiates between MDS defined by genetic abnormalities or by morphologic features (in the form of dysplastic cell lineages), 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 individuals 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 (e.g., 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 individuals with primary MDS or secondary AML to account for chromosomal abnormalities frequently seen in MDS. This system stratifies individuals 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.

#### Myelodysplastic Syndrome Treatment

Treatment of non-progressing MDS has previously 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

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

available to treat MDS, including hematopoietic growth factors (e.g., erythropoietin, darbepoetin, granulocyte colony-stimulating factor), transcriptional-modifying therapy (e.g., U.S. Food and Drug Administration (FDA) hypomethylating agents, nonapproved histone deacetylase inhibitors), immunomodulators (e.g., lenalidomide, thalidomide, antithymocyte globulin, cyclosporine A), low-dose chemotherapy (e.g., 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 individuals age, performance status, medical comorbidities, the individual's preference, risk category, 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 8,400 myeloproliferative neoplasms are diagnosed annually in the United States. Like MDS, myeloproliferative neoplasms primarily occur in older individuals, with approximately 67% reported in individuals aged 60 years and older.

Myeloproliferative neoplasms are characterized by the slow but progressive expansion of a clone of cells with the potential evolution into a blast crisis similar to AML. Myeloproliferative neoplasms 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 myeloproliferative neoplasms is effective clonal myeloproliferation resulting in peripheral granulocytosis, thrombocytosis, or erythrocytosis that is devoid of dyserythropoiesis, granulocytic dysplasia, or monocytosis.

### Myeloproliferative Neoplasm Classification

Myeloproliferative neoplasms are a subdivision of myeloid neoplasms that includes four classic disorders: chronic myeloid leukemia, polycythemia vera, essential thrombocytopenia, and primary myelofibrosis. The WHO classification also includes chronic neutrophilic leukemia, chronic eosinophilic leukemia not otherwise specified, and myeloproliferative neoplasm unclassifiable. In the 2016 classification, mastocytosis is no longer considered a subgroup of the myeloproliferative neoplasms due to its unique clinical and pathologic features.

### Myeloproliferative Neoplasm Treatment

In indolent, non-progressing 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 thrombocytosis and polycythemia vera, and intermediate- and high-risk primary myelofibrosis.

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

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. 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 individuals who had intermediate- and high-risk myelofibrosis, and demonstrated improvements in spleen volume and OS. 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. In 2019, the FDA also approved fedratinib (Inrebic®) for adults with intermediate-2 or high-risk primary or secondary myelofibrosis based on results from a double-blind, randomized, placebo-controlled trial that found improvement in spleen volume and myelofibrosis-related symptoms.

Myeloablative allo-HCT has been considered the only potentially curative therapy, but because most individuals 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

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer individuals 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. Cord blood transplantation is discussed in detail in evidence review 9.001.

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 recipient 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. Human leukocyte antigens 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 recipient 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 (e.g., 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

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

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 individuals 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 individuals before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the individual's disease is in complete remission. Individuals 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 individuals condition. Individuals 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.

### REGULATORY STATUS

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations.

## IV. RATIONALE

[TOP](#)

### SUMMARY OF EVIDENCE

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

For individuals who have MDS who receive myeloablative conditioning (MAC) or reduced-intensity conditioning (RIC) allo-HCT, the evidence includes systemic reviews, randomized controlled trials (RCTs), and numerous 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 (PFS) rates, which reflect the heterogeneity in individual populations, conditioning regimens, and other factors. Reported estimates for 3- to 5-year OS of 40% to 50% are typical. Evidence from randomized and nonrandomized comparisons has suggested that RIC may be used as a risk-adapted strategy in high-risk individuals who are older and with more comorbidities without significantly worsening OS. RIC appears to be associated with lower rates of non-relapse mortality but higher cancer relapse than MAC HCT. At present, HCT is the only potentially curative treatment option for individuals with MDS. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have myeloproliferative neoplasms who receive MAC or RIC allo-HCT, the evidence includes a systematic review and retrospective observational series. Relevant outcomes are OS, disease-specific survival, and treatment-related mortality and morbidity. Evidence has suggested that RIC may be used as a risk-adapted strategy in high-risk individuals who are older and have more comorbidities without significantly worsening OS. RIC appears to be associated with lower rates of non-relapse mortality but higher cancer relapse than myeloablative HCT. At present, HCT is the only potentially curative treatment option for individuals with myeloproliferative neoplasms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome significantly worsening OS.

### V. DEFINITIONS

[TOP](#)

NA

### VI. BENEFIT VARIATIONS

[TOP](#)

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations are based on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

### VII. DISCLAIMER

[TOP](#)

*Capital Blue Cross' medical policies are developed to assist in administering a member's benefits. These medical policies do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the*

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

*benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.*

### VIII. CODING INFORMATION

[TOP](#)

**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

#### Covered when medically necessary:

Procedure Codes								
38204	38205	38207	38208	38209	38210	38211	38212	38213
38214	38215	38230	38240	38242	S2150			

ICD-10-CM Diagnosis Code	Description
C88.80	Other malignant immunoproliferative diseases not having achieved remission
C88.81	Other malignant immunoproliferative diseases, in remission
C88.90	Malignant immunoproliferative disease, unspecified not having achieved remission
C88.91	Malignant immunoproliferative disease, unspecified, in remission
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.21	Atypical chronic myeloid leukemia, BCR/ABL-negative, in remission
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission
C94.41	Acute panmyelosis with myelofibrosis, in remission
C94.42	Acute panmyelosis with myelofibrosis, in relapse
C94.6	Myelodysplastic disease, not elsewhere classified
D45	Polycythemia vera
D46.0	Refractory anemia without ring sideroblasts, so stated

## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

<b>ICD-10-CM Diagnosis Code</b>	<b>Description</b>
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.Z	Other myelodysplastic syndromes
D47.1	Chronic myeloproliferative disease
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic, and related tissue, unspecified
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic, and related tissue

## IX. REFERENCES

[TOP](#)

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<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

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<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
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## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOYDYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
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## MEDICAL POLICY

<b>POLICY TITLE</b>	<b>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELODYSPLASTIC SYNDROMES AND MYELOPROLIFERATIVE NEOPLASMS</b>
<b>POLICY NUMBER</b>	<b>MP 9.056</b>

### X. POLICY HISTORY

[Top](#)

<b>MP 9.056</b>	<b>02/06/2020 Consensus Review.</b> Verbiage added to match BCBSA policy in the policy statement. Policy guidelines, background, and referenced updated. Coding reviewed and corrected.
	<b>01/04/2021 Consensus Review.</b> No changes to the policy statements. Background, rationale, and references coding reviewed.
	<b>02/24/2021 Consensus Review.</b> No change to policy statements. References and coding reviewed.
	<b>02/16/2022 Consensus Review.</b> Policy statement unchanged. Policy Guidelines revised. NCCN language added. FEP language updated. Background and Rationale updated. References added
	<b>08/16/2022 Administrative Update.</b> ICD10 code C94.6 revised. Effective 10/01/2022.
	<b>02/17/2023 Minor Review.</b> No changes to policy statement, however Policy Guidelines section heavily revised. Background and References updated.
	<b>02/08/2024 Minor Review.</b> Policy statement verbiage changed with same intent. References updated. Coding reviewed. No change to coding.
	<b>08/16/2024 Administrative Update.</b> Added new ICD-10 codes C88.80, C88.81, C88.90, and C88.91. Removed ICD-10 code C88.8. Effective date 10/01/2024.
	<b>11/19/2024 Administrative Update.</b> Removed NCCN statement.
	<b>01/13/2025 Consensus Review.</b> No changes to the policy statements. Background, rationale, and references coding reviewed.

[Top](#)

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