

## 2556: Myelofibrosis Pre-HCT Data

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The Myelofibrosis Pre-HCT Supplemental Data Form (Form 2556) must be completed when the primary diagnosis for HCT is Primary Myelofibrosis (PMF) as reported on the Pre-TED Disease Classification Form (Form 2402). This includes essential thrombocythemia (ET) that has transformed to myelofibrosis (MF) at time of HCT or Polycythemia vera (PV) that has transformed to myelofibrosis (MF) at time of HCT. This form captures DIPSS Prognosis Score, laboratory studies prior to JAK1/JAK2 inhibitor therapy, JAK1/JAK2 inhibitor therapy, laboratory studies at last evaluation prior to HCT and disease assessment at time of HCT.

Myeloproliferative neoplasms (MPN) is a category in the World Health Organization (WHO) classification of myeloid tumors. Subtypes include chronic eosinophilic leukemia, chronic neutrophilic leukemia, essential thrombocythemia (ET), mastocytosis, polycythemia vera (PV), primary myelofibrosis (PMF), etc.

Primary myelofibrosis (PMF) is characterized by a proliferation of predominantly megakaryocytes and granulocytes in the bone marrow (BM) that, in fully developed disease, is associated with reactive deposition of fibrous connective tissue and with extramedullary hematopoiesis. There is an evolution in the natural history of the disease from an initial prefibrotic phase characterized by a hypercellular BM with absent or minimal reticulin fibrosis to a fibrotic phase with marked reticulin or collagen fibrosis in the BM and often osteosclerosis. This fibrotic stage of PMF is characterized by a leukoerythroblastosis in the blood with teardrop-shaped red cells, hepatomegaly and splenomegaly.

Myelofibrosis can develop in patients with pre-existing ET or PV. The criteria for diagnosing post-ET MF or post-PV MF include a prior diagnosis of ET or PV and the subsequent development of two or more features including bone marrow fibrosis; leukoerythroblastosis; new anemia; splenomegaly; or constitutional symptoms (i.e., night sweats, fever, or inappropriate weight loss).

[Links to Sections of the Form:](#)

[Q1-17: DIPSS Prognosis Score](#)

[Q18-33: Pre-HCT JAK1 and JAK2 Inhibitor Therapy](#)

[Q34-71: Laboratory Studies Prior to Therapy](#)

[Q72-76: Laboratory Studies at Last Evaluation Prior to HCT](#)

[Q77-90: Disease Assessment at the Time of HCT](#)

+Manual Updates: +

Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click [here](#) or reference the retired manual section on the [Retired Forms Manuals webpage](#).

Date	Manual Section	Add/ Remove/ Modify	Description
2/ 27/ 19	<a href="#">2556: Myelofibrosis Pre-HCT Data</a>	Remove	Removed text referencing the CMS study for Myelofibrosis. The 2556 and 2557 are required for all patients with Myelofibrosis, not just patients enrolled in the CMS study. The titles of the forms have already been changed to remove CMS study from the title.
10/ 25/ 17	2556: Myelofibrosis CMS Study Pre-HCT Data	Add	Added instructions (highlighted red below) for questions 26-27. Indicate “yes” if the patient was treated with a different JAK1 or JAK2 inhibitor (other than ruxolitinib) and specify the drug in question 27. <b>Also, indicate “yes” if the recipient started and stopped ruxolitinib multiple times prior to HCT. In this case, the center should use questions 26-31 to report each treatment interval not captured in questions 19-25.</b>
10/ 25/ 17	2556: Myelofibrosis CMS Study Pre-HCT Data	Add	Added Ruxolitinib (Jakafi) note box above the instructions for question 18.
10/ 14/ 17	2556: Myelofibrosis CMS Study Pre-HCT Data	Add	Added the following instruction for questions 75-76: <i>The reported value must be in units of cells / <math>\mu</math>L.</i>
1/ 31/ 17	2556: Myelofibrosis CMS Study Pre-HCT Data	Add	Version 1 of the 2556: Myelofibrosis CMS Study Pre-HCT Data section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2556.

*Last modified: 2019/02/27*

## Q1-17: DIPSS Prognosis Score

The prognosis of myelofibrosis patients can be predicted by the Dynamic International Prognostic Scoring System (DIPSS) risk categorization as shown in studies conducted by the International Working Group for Myelofibrosis Research and Treatment. The DIPSS risk factors include patient age, constitutional symptoms, hemoglobin, leukocyte count and circulating blasts.

### Question 1: Specify the maximum DIPSS score the patient ever achieved:

The DIPSS score is based on five variables including patient's age, white blood count (WBC), hemoglobin, peripheral blood blasts and constitutional symptoms. Each variable is assigned a point value which are added together to determine the overall score. Refer to Tables 1 and 2. Report the maximum DIPSS score the patient ever achieved between diagnosis and the start of the preparative regimen (or infusion if no preparative regimen was given) in question 1. Note the maximum score that can be reported is 6.

**Table 1. DIPSS variables**

Prognostic Variable	0 Points	1 Point	2 Points
Age (years)	≤ 65	> 65	
WBC ( $\times 10^9$ / L)	≤ 25	> 25	
Hemoglobin (g / dL)	≥ 10		< 10
Peripheral blood blasts	< 1	≥ 1	
Constitutional symptoms	No	Yes	

**Table 2. DIPSS risk category and prognosis**

DIPSS score	DIPSS risk category	Median OS (years)
0	Low	Not reached
1-2	Intermediate – 1	14.2
3-4	Intermediate – 2	4
5-6	High	1.5

### Question 2: Specify when maximum DIPSS score was documented

Specify whether the maximum DIPSS score was documented “at diagnosis”, “between diagnosis and the preparative regimen” or “at last evaluation prior to the start of the preparative regimen.”

 When completing questions 3-17, report the clinical and laboratory assessments used to determine the maximum DIPSS score. For example, if the maximum DIPSS score was documented at diagnosis, report the testing performed at diagnosis.

### **Question 3-5: WBC**

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time the maximum DIPSS score was documented. If “known,” report the WBC and unit of measure documented on the laboratory report in question 4; indicate the date sample was collected in question 5. If “unknown,” continue with question 6.

### **Question 6-8: Hemoglobin**

Indicate whether the hemoglobin count is “known” or “unknown” at the time the maximum DIPSS score was documented. If “known,” report the hemoglobin and unit of measure documented on the laboratory report in question 7 and the date of sample collection in question 8. If “unknown,” continue with question 10.

### **Question 9: Were RBC transfused < 30 days before date of test?**

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused *less than or equal to* 30 days prior to the testing.

### **Question 10-12: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time when the maximum DIPSS score was documented. If “known,” report the platelet count and unit of measure documented on the laboratory report in question 11 and the date of sample collection in question 12. If “unknown,” continue with question 14.

### **Question 13: Were platelets transfused < 7 days before date of test?**

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused *less than or equal to* 7 days prior to the testing.

### **Question 14-16: Blasts in blood**

Indicate whether the percentage of blasts in the blood is “known” or “unknown” at the time of when the

maximum DIPSS score was documented. If “known,” report the blast percentage documented on the laboratory report in question 15 and the date of sample collection in question 16. If “unknown,” continue with question 17.



If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

**Question 17: Did the recipient have constitutional symptoms? (>10% weight loss in 6 months, night sweats, unexplained fever higher than 37.5C)**

If there was evidence of constitutional symptoms at the time the maximal DIPSS score was documented, select “yes”. If there was no evidence of constitutional symptoms, select “no.” If documentation is not clear or is not available to determine if constitutional symptoms were present, select “unknown.”

*Last modified: 2017/01/31*

## Q18-33: Pre-HCT JAK1 and JAK2 Inhibitor Therapy

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Janus associated kinase inhibitors, also known as JAK inhibitors, are a type of medication that inhibits the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2) thereby blocking an enzyme that causes scar tissue to form in the bone marrow. These inhibitors are indicated for treatment of patients with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF.

Examples of JAK inhibitors include ruxolitinib (Jakafi / Jakavi) and tofacitinib (Xeljanz / Jakvinus).



### Ruxolitinib (Jakafi)

If the recipient started and stopped ruxolitinib (Jakafi) therapy multiple times prior to transplant, report the most recent treatment interval in questions 19-25. Also, report the prior treatment interval(s) in questions 26-31.

Do not, however, report ruxolitinib (Jakafi) treatments given for past transplants that have previously been reported.

### Question 18: Did the recipient receive JAK1 or JAK2 inhibitor therapy? (pre-HCT)?

Indicate “yes” if the recipient received JAK1 or JAK2 therapy prior to the current HCT (not including therapy given for past HCTs that have previously been reported) and continue with question 19. If “no,” continue with question 34.

### Question 19: Ruxolitinib (Jakafi)

Indicate “yes” if the recipient received ruxolitinib, a Janus kinase inhibitor with selectivity for JAK1 and JAK2 of this enzyme and continue with question 20. Indicate “no” if the recipient did not receive ruxolitinib and continue with question 26.

### Question 20-21: Date therapy started

Indicate “known” if the therapy start date is documented, and specify the first date of ruxolitinib therapy administration in question 21. If the date is unknown, indicate such and continue with question 22.

### Question 22-23: Date therapy stopped

Indicate “known” if the therapy completion date is documented and specify the date therapy stopped in

question 23. If the patient is receiving systemic therapy in cycles, specify the *first day of the last cycle* of systemic therapy. If the treatment is not given in cycles (e.g., daily), indicate the last day systemic therapy was administered.

If the date is unknown, indicate such and continue with question 26.

#### **Question 24-25: Specify reason therapy stopped**

Indicate why the ruxolitinib therapy was stopped from the list of reasons provided. If “Other” is checked, specify “other reason” in question 25.

#### **Question 26-27: Other JAK1 or JAK2 inhibitor**

Indicate “yes” if the patient was treated with a different JAK1 or JAK2 inhibitor (other than ruxolitinib) and specify the drug in question 27. Also, indicate “yes” if the recipient started and stopped ruxolitinib multiple times prior to HCT. In this case, the center should use questions 26-31 to report each treatment interval not captured in questions 19-25.

If “no,” continue with question 32.

#### **Question 28-29: Date therapy started**

Indicate “known” if the therapy start date is documented, and specify the first date of systemic therapy administration in question 29. If the date is “unknown”, indicate such and continue with question 30.

#### **Question 30-31: Date therapy stopped**

Indicate “known” if the therapy completion date is documented. Continue with question 31 and specify the date therapy stopped. If the patient is receiving systemic therapy in cycles, specify the *first day of the last cycle* of systemic therapy. If the treatment is not given in cycles (e.g., daily), indicate the last day systemic therapy was administered.

If the date is unknown, indicate such and continue with question 32.

The FormsNet3<sup>SM</sup> application allows questions 26-33 to be reported multiple times. Complete these questions for each JAK1 or JAK2 inhibitor therapy administered prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given).

#### **Question 32: Response to therapy**

For each line of therapy given, indicate if there was “clinical improvement”, “stable disease”, “non-splenic disease progression”, “splenic disease progression” or “transformation to leukemia”.

**Clinical improvement:** defined as 50% improvement in palpable spleen length for spleen palpable by 10 cm, or complete resolution of splenomegaly for palpable spleen <10 cm

**Non-splenic disease progression:** increase in blasts to 10% to 19%, intolerance to treatment due to hematologic/non-hematologic side effects, or new onset transfusion-requiring anemia

**Splenic disease progression:** appearance of new splenomegaly palpable 5 cm below costal margin (BCM) or 100% increase in palpable distance BCM for baseline splenomegaly of 5 cm to 10 cm BCM, 50% increase in palpable distance BCM for baseline splenomegaly of 10 cm BCM, loss of spleen response, or symptomatic splenomegaly requiring splenectomy

**Transformation to leukemia:** peripheral blood or bone marrow blast count of 20%

### Question 33: Date assessed

Report the date of the response to therapy reported in question 32 was assessed. Report the date of the pathological evaluation (e.g., bone marrow biopsy) or clinical evaluation. Enter the date the sample was collected for pathological and/or laboratory evaluation or report the date of the office visit in which the physician clinically assessed the recipient's response.

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## Q34-71: Laboratory Studies Prior to Therapy

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Specify the laboratory values immediately prior to JAK1 / JAK2 inhibitor therapy. If no JAK1 / JAK2 inhibitory therapy was given, report results at last evaluation prior to the start of the preparative regimen for HCT.

### **Question 34-35: Was presence of somatic mutations tested? (immediately prior to JAK1 / JAK2 inhibitor therapy initiation or prior to the start of the preparative regimen if no JAK1 / JAK2 inhibitor therapy was given)**

Testing for somatic mutations may be performed by different methods including next generation sequencing, polymerase chain reaction, microarray, and fluorescence in situ hybridization. If testing was performed by any / all of these methods prior to the start of JAK1 / JAK2 inhibitor therapy was given (or prior to the start of the preparative regimen if no JAK1 / JAK2, capture the most recent test(s) in questions 37-56.

Indicate “yes” if somatic mutations were tested for and specify the date the sample was collected in question 35. Indicate “no” if somatic mutations were not tested for or “unknown” and go to question 57.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

### **Question 36: Specify sample source**

Indicate if the sample was from “bone marrow” or from “peripheral blood”.

### **Question 37-54: Was presence of somatic mutations tested? (immediately prior to JAK1 / JAK2 inhibitor therapy initiation)**

For each gene mutation listed, Indicate “positive”, “negative” or “not done”.

### **Question 55-56: Other gene mutation**

Indicate “positive” or “negative” if another gene mutation was tested for that was not listed in questions 37-54, and specify the other gene in Q56. If another gene mutation was not tested for, indicate “not done” and go to question 57.

### **Question 57-59: WBC**

Indicate whether the white blood count (WBC) is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the WBC and unit of measure documented on the laboratory report in question 58; indicate the date sample was collected in question 59. If “unknown,” continue with question 60.

**Question 60-62: Hemoglobin**

Indicate whether the hemoglobin value is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the hemoglobin and unit of measure documented on the laboratory report in question 61 and the date of sample collection in question 62. If “unknown,” continue with question 64.

**Question 63: Were RBC transfused < 30 days before date of test?**

Transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support the counts.

Indicate if red blood cells were transfused *\_less than or equal t\_o* 30 days prior to the testing.

**Question 64-66: Platelets**

Indicate whether the platelet count is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the platelet count and unit of measure documented on the laboratory report in question 65 and the date of sample collection in question 66. If “unknown,” continue with question 68.

**Question 67: Were platelets transfused < 7 days before date of test?**

Transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support the counts.

Indicate if platelets were transfused *less than or equal to* 7 days prior to the testing.

**Question 68-70: Blasts in blood**

Indicate whether the percentage of blasts in the blood is “known” or “unknown” at the time of last evaluation prior to therapy. If “known,” report the blast percentage documented on the laboratory report in question 69 and the date of sample collection in question 70. If “unknown,” continue with question 71.



If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and “0” can be entered on the form.

**Question 71: Did the recipient have constitutional symptoms? (>10% weight loss in 6 months, night sweats, unexplained fever higher than 37.5C)**

If there was evidence of constitutional symptoms at time of last evaluation prior to therapy, select “yes”. If there was no evidence of constitutional symptoms, select “no.” If documentation is not clear or is not

available to determine if constitutional symptoms were present, select “unknown.”

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# Q72-76: Laboratory Studies at Last Evaluation Prior to HCT

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## Question 72-74: Total serum ferritin

Ferritin is a blood cell protein that contains iron. Ferritin levels indicate how much iron a person's body is storing. If the ferritin level is lower than normal, it indicates the body's iron stores are low (iron deficiency). If the ferritin level is higher than normal it could indicate hemochromatosis, a condition that causes the body to store too much iron. Other causes of an elevated ferritin level include liver disease, acute and chronic inflammatory conditions, malignancy to name a few.

Indicate whether the total serum ferritin value is "known" or "unknown" at the time of last evaluation prior to the start of prep for HCT. If "known", report the ferritin value documented on the laboratory report in question 73 and the date of sample collection in question 74. If "unknown", continue with question 75.

## Question 75-76: CD34+ cells (peripheral blood)

Indicate whether the CD34+ cell count is "known" or "unknown" at the time of last evaluation prior to the start of prep for HCT. If "known", report the CD34+ cell count documented on the laboratory report in question 76. The reported value must be in units of cells /  $\mu$ L.

*Last modified: 2017/10/14*

# Q77-90: Disease Assessment at the Time of HCT

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## Question 77: Did the recipient have evidence of pulmonary hypertension at HCT?

Pulmonary hypertension (PH) refers to elevated pulmonary arterial pressure. PH can be due to a primary elevation of pressure in the pulmonary arterial system alone (pulmonary arterial hypertension), or secondary to elevations of pressure in the pulmonary venous and pulmonary capillary systems (pulmonary venous hypertension; post-capillary PH).

Indicate “yes” if the recipient has evidence of PH at the time of HCT or “no” if they did not. If documentation is not clear or is not available to determine if PH was present, select “unknown.”

## Question 78: Did the recipient have evidence of portal hypertension at HCT?

Portal hypertension is high blood pressure in the hepatic portal system, which includes the portal vein and its branches. The hepatic portal system drains most of the intestines to the liver.

Indicate “yes” if the recipient has evidence of portal hypertension at the time of HCT or “no” if they did not. If documentation is not clear or is not available to determine if portal hypertension was present, select “unknown.”

## Question 79: Hepatomegaly

Hepatomegaly is an enlargement of the liver. Indicate “yes” if the recipient has evidence of hepatomegaly at the time of HCT, and continue with question 80. Indicate “no” if they did not and go to question 82.

## Question 80: Specify the liver size

Specify the number of centimeters the liver is below the right costal margin.

## Question 81: Specify the method used to measure the liver size

Indicate if the liver size was measured by “physical assessment”, “ultrasound” or “CT scan”

## Question 82-83: Spleen size

If the spleen size is “known” indicate the number of centimeters below the left lower costal margin in question 83. If the spleen size is “unknown” or “not applicable” ( due to splenectomy), indicate the appropriate option and go to question 84.

**Question 84: Iron overload**

Indicate “yes” if the patient has documented iron overload and go to question 85. Indicate “no” if the patient doesn’t have documented iron overload and go to Signature Lines.

**Question 85: Serum ferritin**

Ferritin is a blood cell protein that contains iron. A ferritin level indicates how much iron a person’s body is storing. If the ferritin level is lower than normal, it indicates the body’s iron stores are low (iron deficiency). If the ferritin level is higher than normal it could indicate hemochromatosis, a condition that causes the body to store too much iron. Other causes of an elevated ferritin level include liver disease, acute and chronic inflammatory conditions, malignancy to name a few.

Indicate “yes” if the serum ferritin level indicated iron overload or “no” if it did not or wasn’t performed.

**Question 86: Liver MRI**

Indicate “yes” if a liver MRI was used to make the diagnosis iron overload or “no” if it did not or wasn’t performed.

**Question 87-88: Other method**

Indicate “yes” if another method was used to make the diagnosis of iron overload and indicate the method in question 88. Indicate “no” if another method was not used to make the diagnosis of iron overload.

**Question 89: Iron chelation therapy**

Iron chelation therapy is the removal of excess iron from the body using drugs such as deferoxamine.

Indicate “yes” if iron chelation therapy was used to treat the iron overload or “no” if it was not.

**Question 90: Phlebotomy**

Indicate “yes” if phlebotomy was used to treat the iron overload or “no” if it was not.

**Signature Lines:**

The FormsNet3<sup>SM</sup> application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.

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