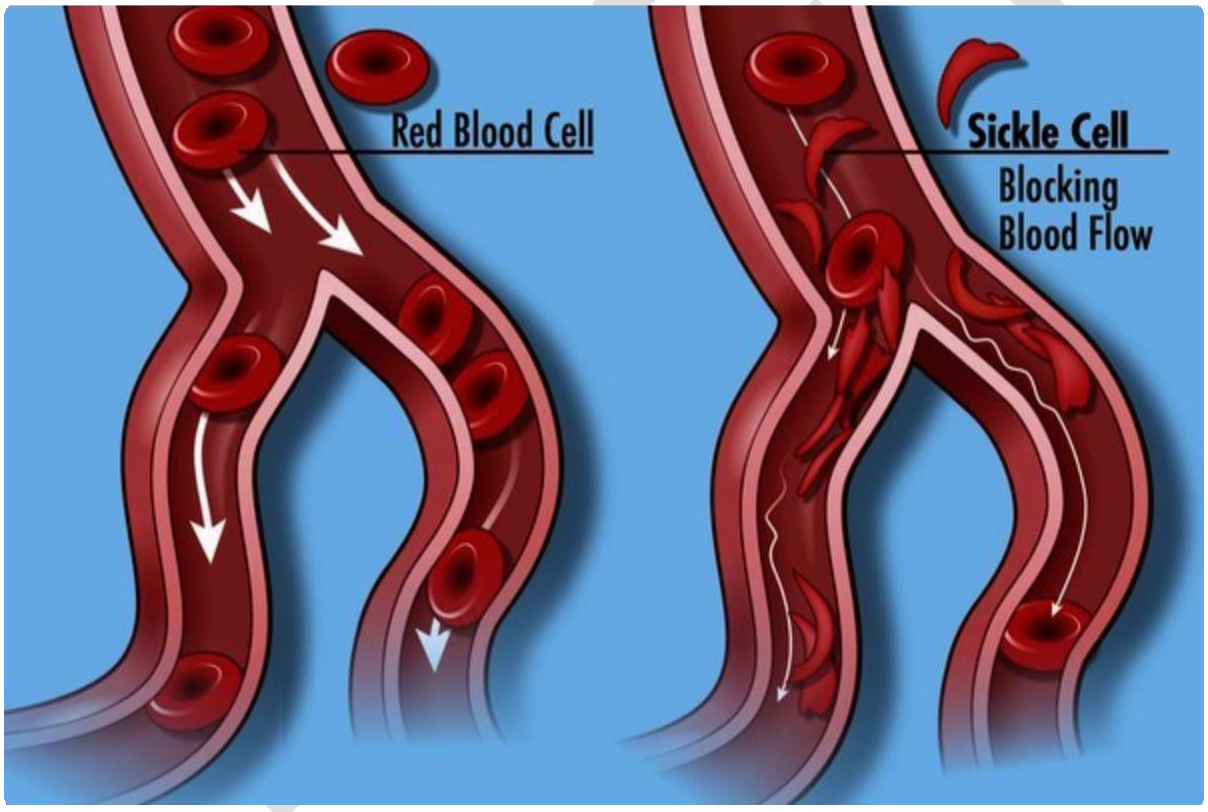
2030/2130: Sickle Cell Disease (SCD)

Sickle Cell Disease (SCD) is a group of disorders that adversely affect the body's production of hemoglobin, the component in red blood cells that delivers oxygen throughout the body.[1] Individuals with these disorders possess atypical hemoglobin molecules, called hemoglobin "S," which can distort the red blood cell morphology into a sickle, or crescent, shape. Multiple variants of SCD exist and each genetic sub-type is characterized by different prognostic indications.

Graphic 1. Depiction of a Sickle Cell



SCD is often diagnosed at birth following newborn screening or following severe and / or persistent infections. Symptoms of sickle cell disorders include anemia (low red blood cell counts) as a result of the sickle cells dying prematurely, repeat infections, and periodic episodes of pain (i.e., pain crisis). The severity of symptoms varies from person to person ranging from mild to severe. Refer to *Table 1. Sickle Cell Disease Symptoms* for additional symptoms

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associated with SCD. Hematopoietic cell transplant (HCT) is currently the major curative treatment for SCD.

Table 1. Sickle Cell Disease Symptoms[2]

Common SCD Symptoms
100% of people have these symptoms:
Chronic hemolytic anemia
80 – 99% of people have these symptoms:
Recurrent infections
30 – 79% of people have these symptoms:
Abnormality of the spleen
Avascular necrosis
Chest pain
Leukocytosis
Osteomyelitis
Osteoporosis
Pigment gallstones
Reticulocytosis
Thrombocytosis
5 – 29% of people have these symptoms:
Abnormality of the nervous system
Cholestasis
Elevated serum creatinine
Hypoxemia

DRAFT

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Increased LDH activity
Persistence of hemoglobin F
Unconjugated hyperbilirubinemia
1 – 4% of people have these symptoms:
Increased mean corpuscular volume
Microcytic anemia
Additional symptoms that recipients may experience:
Abdominal pain
Cardiomegaly
Hematuria
Hepatomegaly
Hypertension
Jaundice
Priapism
Renal insufficiency
Retinopathy
Splenomegaly
Stroke

DRAFT

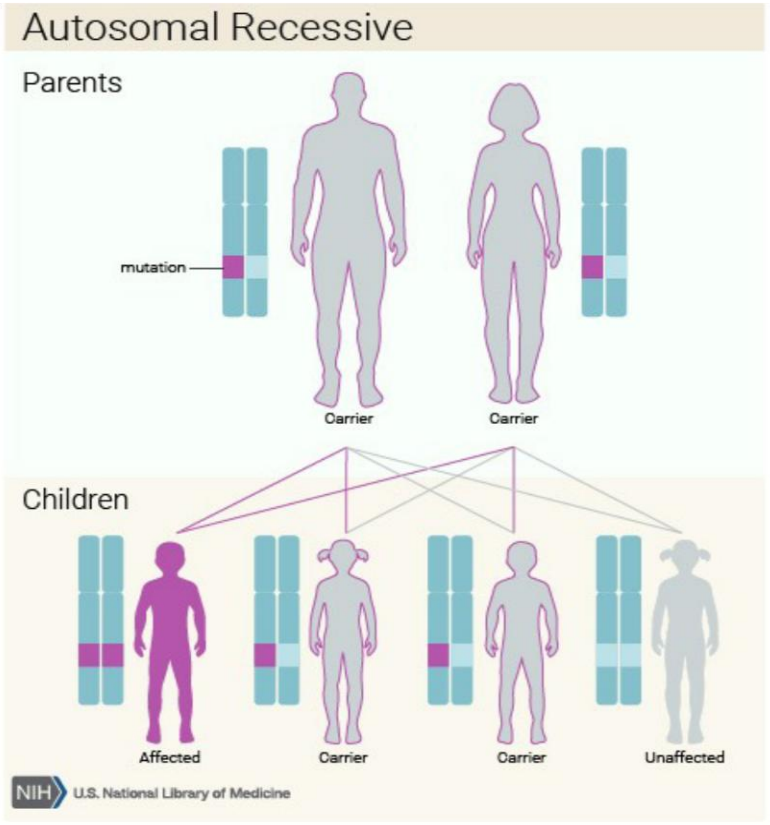
The table above contains information collected from the Human Phenotype Ontology (HPO) database.

SCD is inherited in an autosomal, recessive pattern. A person who carries one copy of the mutated gene is said to be a carrier of the sickle cell trait but will not exhibit symptoms of SC. If

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two people are both carriers for the sickle cell trait and have a child, there is a 25% chance that this child will have SCD, a 50% chance of being a carrier, and a 25% chance that the child will not be a carrier nor have SCD. Reference *Graphic 2. Inheritance of Sickle Cell Disease* below for a depiction of this description:

Graphic 2. Inheritance of Sickle Cell Disease



- 2030: Sickle Cell Disease (SCD) Pre-HCT
- 2130: Sickle Cell Disease (SCD) Post-HCT

[1] Genetics Home Reference: Your Guide to Understanding Genetic Conditions. 2020. *Sickle Cell Disease*. [online] Available at: < https://ghr.nlm.nih.gov/condition/sickle-cell-disease > .

[2] Genetics Home Reference: Your Guide to Understanding Genetic Conditions. 2020. *Sickle Cell Disease*. [online] Available at: < https://ghr.nlm.nih.gov/condition/sickle-cell-disease >.

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Instructions for Sickle Cell Disease Pre-Infusion Data (2030)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Sickle Cell Disease Pre-Infusion Data.

2030: SCD Pre-Infusion

SCD Pre-Infusion Data

The SCD Pre-Infusion Data Form (2030) Form is one of the Comprehensive Report Forms. This form captures SCD-specific pre-infusion data such as disease classification at diagnosis, transfusion status prior to the start of the preparative regimen, organ assessments prior to the start of the preparative regimen, and the indication for transplant.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Disease Classification Form (2402) Form as **Sickle Cell Disease (SCD)**.

Links to Sections of the Form

Q1: Subsequent Infusion
Q2-3: Sickle Cell Diagnosis
Q4-14: Transfusion Therapy
Q15-17: Therapy for Iron Overload
Q18-23: Pulmonary Assessments
Q24-41: Cardiovascular Assessments
Q42-47: Renal Assessments
Q48-52: Splenic Assessments
Q53-57: Acute Chest Syndrome
Q58-61: Pain
Q62-69: Avascular Necrosis
Q70-79: Central Nervous System
Q80-90: Other Symptoms
Q90-102: Existing Organ Impairments
Q103-104: Infection

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Q105-111: Disease Modifying Therapies
Q112-137: Other Laboratory Studies
Q138-139: Reason for Infusion
Q140: Marrow Evaluation at Last Evaluation

Manual Updates:

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

To review the historical Manual Change History for this manual, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
11/19/2026	Sickle Cell Disease Pre-Infusion (2030)	Add	Version 4 of the 2030: Sickle Cell Disease Pre-Infusion section of the Forms Instructions Manual released. Version 4 corresponds to revision 6 of the Form 2030.

Q1: Subsequent Infusion

Question 1: Is this the report of a second or subsequent infusion?

Report **No** and go to *Was sickle cell disease diagnosed at birth?* in any of the following scenarios:

- This is the first infusion reported to the CIBMTR; or
- This is a second or subsequent infusion for a different disease (i.e., the patient was previously transplanted for a disease other than Sickle Cell Disease); or
- This is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (i.e., the patient was on the TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

Report **Yes** and go to *Were any red blood cell (RBC) transfusions administered?* if this is a subsequent infusion for the same disease ***and*** the baseline SCD disease insert was completed previously.

Section Updates

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Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q2 – 3: Sickle Cell Diagnosis

Findings Prior to Infusion

When reporting data on the Sickle Cell Disease (SCD) Pre-Infusion Data (2030) Form, report all findings at any time prior to the start of the preparative regimen, unless otherwise specified. If no preparative regimen was given, report all findings at any time prior to infusion (day 0).

Questions 2 – 3: What is the recipient's sickle cell disease genotype?

Genetics play a critical role in the development of sickle cell disorders. Clinical symptoms vary depending on which gene variants are inherited. Accurate identification of the recipient's sickle genotype may help guide clinical management of symptoms.

Specify the recipient's sickle cell disease genotype. If the recipient exhibits a sickle cell genotype that is not listed, select **Other genotype** and specify the sickle cell genotype in question 5.

See *Table 1. Sickle Cell Genotypes* below for a description and common characteristics of each genetic variant.

Table 1. Sickle Cell Genotypes

Genotype	Description
Hb SC	One hemoglobin S gene is inherited from one parent and one abnormal hemoglobin-producing "C" gene is inherited from the other parent. Typically characterized by mild symptoms but increased likelihood of proliferative sickle retinopathy has been observed.
Hb SD	One hemoglobin S gene is inherited from one parent and one abnormal hemoglobin-producing "D" gene is inherited from the other parent. The severity of symptoms varies for recipients with this genotype.
Hb SO	A rare, compound, heterozygous hemoglobinopathy characterized by inheritance of one hemoglobin S gene from one parent and one abnormal hemoglobin-producing

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Arab	"O" gene inherited from the other parent. Severity is similar to those of homozygous SCD.
Hb SS	Most common type of sickle cell disease and is often called homozygous sickle cell anemia. One hemoglobin S gene is inherited from each parent. Often characterized by higher prevalence of hemolysis and lower hemoglobin values compared to Hb SC or beta+ thalassemia. Incidence of leg ulcers, stroke, episodes of priapism are increased. Regarded as a severe form of SCD.
Hb S beta^0 thalassemia	A more severe form of SCD characterized by crescent-shaped red blood cells (RBC) (e.g., sickle cells) that break down prematurely as well as populations of smaller RBCs, simultaneously.
Hb S beta[+] thalassemia	A mild form of SCD characterized by crescent-shaped red blood cells (RBC) (e.g., sickle cells) that break down prematurely as well as populations of smaller RBCs, simultaneously.
Hb S delta beta^0 thalassemia	A rare, homozygous hemoglobinopathy characterized by decreased production of the delta- and beta-globin chains. There is a compensatory increase in the production and expression of Hb F in affected individuals.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q4 – 13: Transfusion Therapy

Question 4: Were any red blood cell (RBC) transfusions administered?

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Red blood cell (RBC) transfusions are often given as supportive care to lower hemoglobin S for recipients diagnosed with SCD.

Indicate if the recipient received any RBC transfusions between diagnosis and the start of the preparative regimen / infusion. If RBCs were transfused, select **Yes**. If the recipient did not receive any RBC transfusions or no information is available to determine if the recipient received RBC transfusions between diagnosis and the start of the preparative regimen / infusion, report **No**.

Question 5: Number of RBC transfusion events within the last 12 months

Transfusions may be referred to as "simple" or "exchange" transfusions. A simple transfusion refers to a direct infusion of a blood product. An exchange transfusion refers to the slow removal and replacement of the recipient's blood with that of a healthy donor's blood. A transfusion event consists of one or more RBC unit(s) given in a day.

Indicate the total number of RBC transfusion events the recipient received within 12 months prior to the start of the preparative regimen / infusion to prevent sickle-related vaso-occlusive events.

- **Example**: The progress notes state a recipient was transfused with one RBC unit for each month, for six months. The number of transfusions increased, and the recipient receives two RBC units on the same day, each month, for the following six months prior to the start of the preparative regimen. The total number of RBC transfusion events within the last 12 months would be reported as "12."

Question 6: Date of last transfusion administered *(answer ONLY if a transfusion was administered within the last 12 months)*

Report the date of the *most recent* RBC transfusion administered prior to the start of the preparative regimen / infusion.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 7: Was a transfusion administered to PREVENT sickle cell related events? *(includes simple or exchange transfusions)*

Transfusions administered routinely to offset the effects of sickle cell-related events are often called "chronic transfusions" within progress notes. In the context of reporting, "chronic transfusions" are defined as eight or more transfusion events per year, for at least a year, or a lifetime cumulation of ≥ 20 transfusion events between diagnosis and referral for transplant.

If any of the red blood cell transfusions were administered to prevent sickle cell related events, report **Yes**.

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Report **No** in the following scenarios:

- If the recipient did not receive transfusions to prevent sickle cell related events.
- There is no information available to determine if the recipient received transfusions to prevent sickle cell-related events.
- If the recipient is receiving transfusion therapy for reasons other than to prevent sickle cell-related events.

Questions 8 – 9: Date transfusion started

Indicate if the date transfusion(s) administered to prevent sickle cell related events began is **Known**. If **Known**, enter the date when the first transfusion began. If transfusions were given over multiple days, report the first date of administration where the intent of transfusion was to offset or prevent the effects of sickle cell-related events. The reported start date should align with the recipient's sickle cell-related event for which the transfusion was administered and may not be the same transfusion event reported in *Date of last transfusion administered*. If the reported transfusion start date is an estimated date, also select **Date estimated**.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 10 – 11: Date transfusion stopped

Indicate if the transfusion therapy stop date is **Known**. If the therapy stop date is **Known**, enter the date when the transfusion(s) to prevent sickle cell related events stopped. If the reported transfusion start date is an estimated date, also select **Date estimated**.

If the recipient is still receiving transfusions to prevent sickle cell related events at the start of the preparative regimen / infusion, report **Not applicable**.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 12: Are the RBC units used for transfusion of an extended phenotype match (D, C, c, E, e, K)? *(includes partial extended phenotype matches)*

Extended phenotype testing may be performed on RBC units prior to transfusion to ensure donor and recipient matches are confirmed beyond the standard ABO compatibility matching to decrease the risk of alloimmunization. This information is typically found within the blood bank section of the medical record.

Report **Yes** if the RBC unit(s) used for transfusion are of an extended phenotype match (particularly D, C, c, E, e, or K). If the RBC unit(s) used for transfusion were not matched for extended phenotype D, C, c, E, e, or K or it is unknown if matched, report **No**.

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Questions 13 – 14: Are RBC alloantibodies present?

The presence of RBC alloantibodies may cause serologic incompatibility and make the selection of RBC units for future transfusions difficult. RBC alloantibodies are typically present once alloimmunization has occurred.

If RBC alloantibodies are present prior to the start of the preparative regimen / infusion, report **Yes** and specify the number of alloantibodies identified. If testing for RBC alloantibodies were performed multiple times prior to the start of the preparative regimen / infusion, report the most recent assessment.

If RBC alloantibodies were not present prior to the start of the preparative regimen / infusion, report **No**. Report **Unknown** if testing was not performed or it is not known if alloantibodies were present.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q15 – 17: Therapy for Iron Overload

Question 15: Was iron chelation therapy received at any time?

Iron chelation therapy is used to prevent or reduce iron overload. Examples include, but are not limited to, Deferoxamine (Desferal) and Deferasirox (Jadenu, Exjade).

Indicate if iron chelation therapy was administered at any time between diagnosis and the start of the preparative regimen / infusion. If iron chelation therapy was not given or if no information is available to determine if iron chelation therapy was given at any time between diagnosis and the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Questions 16 – 17: Specify therapy *(check all that apply)*

Specify the iron chelation therapy(ies) administered to reduce iron overload. Select all that apply. If the administered agent is not listed, select **Other** and specify the agent.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

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Q18 – 23: Pulmonary Assessments

Question 18: Were pulmonary function tests (PFT) performed? *(If PFT tests were conducted we ask that you attach the most recent report)*

Pulmonary function tests (PFTs) are non-invasive breathing evaluations that measure how much air your lungs can hold, how fast you can move air in and out, and how well your lungs transfer oxygen into your bloodstream. Indicate if pulmonary function tests (PFTs) were performed at any time between diagnosis and the start of the start of the preparative regimen / infusion.

If PFTs were not performed or unknown if PFTs were performed between diagnosis and the start of the preparative regimen / infusion, select **No**.

WARRIOR-SCD
Attaching the report (when available) is required for WARRIOR-SCD.

Question 19: Indicate if the PFT report is attached

Indicate if the PFT report was **Attached** in FormsNet3^{SM}. If multiple PFTs were performed between diagnosis and the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Children unable to perform PFTs
This question is only applicable for recipients ≤ 5 years of age.

Question 20: For children unable to perform a PFT, was oxygen saturation on room air > 95%? *(only required to answer if children are 5 years of age or less)*

Indicate if oxygen saturation on room air was > 95% between diagnosis and the start of the preparative regimen / infusion. If oxygen saturation is > 95%, report **Yes**. If the oxygen saturation on room air was ≤ 95%, report **No**. If oxygen saturation was assessed multiple times, report based on the most recent assessment prior to the start of the preparative regimen.

If oxygen saturation was not assessed at any time between diagnosis and prior to the start of the preparative regimen / infusion, report **Not done**.

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Questions 21 – 22: Was a 6-minute walk test performed?

A 6-minute walk test is used to assess total distance walked within 6 minutes to determine aerobic capacity and endurance. Indicate if a 6-minute walk test was performed at any time between diagnosis and the start of the preparative regimen / infusion. If **Yes**, report the total distance walked and specify the unit of measure. If multiple walk tests were performed between diagnosis and the start of the preparative regimen / infusion, report the results of the most recent assessment.

If a 6-minute walk test was not performed, recipient is unable to walk, or cannot perform the 6-minute walk test due to their current clinical status, report **No**.

If no information is available to determine if a 6-minute walk test was performed at any time between diagnosis and the start of the preparative regimen / infusion, report **Unknown**.

WARRIOR-SCD
Attaching the report is required for WARRIOR-SCD.

Questions23: Indicate if the 6-minute walk test report is attached

Indicate if documentation of the 6-minute walk test was **Attached** in FormsNet3^{SM}. If multiple 6-minute walk tests were performed, attach the most recent report between diagnosis and the start of the preparative regimen / infusion. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q24 – 41: Cardiovascular Assessments

Figure 1: Echocardiogram

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M-MODE					
LV Diastolic Diameter	23.8 mm	37-56	Posterior wall	4.3 mm	8-12
LV Systolic Diameter	13.7 mm		LV_Mass	16.7 g	
LV Ejection Fraction Teich	76 %		Aortic Sinuses	10.6 mm	=<37
Interventricular septum	3.9 mm	8-12	LA Systolic Diameter	16.4 mm	=<40
DOPPLER					
AV Peak Velocity	114 cm/s		PV Peak Velocity	99.1 cm/s	
AV Peak Gradient	5.2 mmHg		PV Peak Gradient	3.9 mmHg	
LVOT Peak Velocity	108 cm/s				

LV: There is normal situs. Normal LV size and systolic function. The heart is displaced inferiorly but structurally normal. The ventricular septum appears intact and there is no shunting noted. The LVEDD normal range is 2.11 - 2.92 Z is -0.64. IVS normal range is 0.36 - 0.63 Z is -1.56. PW normal range is 0.35 - 0.58 Z is -0.60.

RV: Normal RV size and systolic function.

Atria: The atria are of normal size. The atrial septum appears intact and there is no shunting noted.

AV: The aortic valve is tricuspid and normal.

MV: Structurally normal mitral valve.

TV&PV: The tricuspid valve is normal. There is trace tricuspid regurgitation. The pulmonary valve is normal with normal doppler flow.

Aorta: Normal sized aortic sinuses and proximal ascending aorta. The arch, and descending aorta are normal. Th AoR normal range is 0.93 - 1.43 Z is -1.07

Peri: No pericardial effusion.

IVC: Normal

Questions 24 – 26: Was left ventricular ejection fraction (LVEF) or left ventricular shortening fraction reported by echocardiogram?

The left ventricular ejection fraction (LVEF) is a percentage that represents the volume of blood pumped from the left ventricle into the aorta (also known as stroke volume) compared to the volume of blood in the ventricle just prior to the heart contraction (also known as end diastolic volume). The left ventricular shortening fraction is the percentage change in cavity dimensions of the left ventricle with systolic contraction. The LVEF and left ventricular shortening fraction are assessed via an echocardiogram. Refer to Figure 1 above for an example of an echocardiogram report.

Report **Yes** if *either* LVEF or left ventricular shortening fraction was assessed at any time between diagnosis and the start of the preparative regimen / infusion and provide the

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percentage(s). If the LVEF *and* left ventricular shortening fraction were assessed, report the results of both. If the LVEF and/or left ventricular shortening fraction were assessed multiple times between diagnosis and the start of the preparative regimen / infusion, report the most recent value(s).

If LVEF and/or left ventricular shortening fraction were not assessed or if no information is available to determine if LVEF and/or left ventricular shortening fraction were assessed at any time between diagnosis and the start of the preparative regimen / infusion, report **No**.

Questions 27 – 28: Is there evidence of pulmonary hypertension?

Pulmonary hypertension (PH) refers to elevated pulmonary arterial pressure and is diagnosed either by an echocardiogram or right heart catheterization. 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 had evidence of PH at any time between diagnosis and the start of the preparative regimen and select which method was used to diagnose PH.

If the recipient did not have evidence of PH at any time between diagnosis and the start of the preparative regimen, or if no information is available to determine if the recipient had PH, report **No**.

WARRIOR-SCD
Attaching the report is required for WARRIOR-SCD.

Question 29: Indicate if the echocardiogram report is attached

Indicate if the echocardiogram was **Attached** in FormsNet3^{SM}. If multiple echocardiograms were performed between diagnosis and the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Attaching Right Heart Catheterization Report
This question is only applicable to WARRIOR-SCD

WARRIOR-SCD
Attaching the report is required for WARRIOR-SCD.

Questions 30: Indicate if the right heart catheterization report is attached

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Indicate if the right heart catheterization was **Attached** in FormsNet3^{SM}. If multiple right heart catheterizations were performed between diagnosis and the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 31– 32: Cardiac iron T2 imaging *(found on MRI results)*

Cardiac T2 mapping is a noninvasive MRI method that is used to identify myocardial iron accumulation in several iron storage diseases. Indicate if the cardiac iron T2 imaging is **Known**. If **Known**, specify the value and unit of measure from the MRI results in m/sec. If the cardiac iron T2 imaging was done multiple times between diagnosis and the start of the preparative regimen / infusion, report the most recent assessment.

Attaching Cardiac MRI Report
This question is only applicable to WARRIOR-SCD

WARRIOR-SCD
Attaching the report is required for WARRIOR-SCD.

Question 33: Indicate if the cardiac MRI report is attached

Indicate if the cardiac MRI was **Attached** in FormsNet3^{SM} . If multiple cardiac MRIs were performed between diagnosis and the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 34 – 36: Was brain natriuretic peptide (BNP) assessed?

Brain natriuretic peptide (BNP) is a hormone secreted by cardiac ventricle cells in response to increased ventricular blood volume. BNP is typically measured using various immunoassay techniques. Confirm with the attending physician on where to locate immunoassay results measuring BNP, if available.

Indicate if BNP was assessed at any time between diagnosis and the start of the preparative regimen / infusion. If **Yes**, report the value as documented on the laboratory report (in pg / mL) and the date the sample was collected. If BNP was assessed multiple times between diagnosis and the start of the preparative regimen / infusion, report the results of the most recent test. If BNP was not assessed or if no information is available to determine if BNP was assessed

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between diagnosis and the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 37 – 39: N-terminal pro b-type natriuretic peptide (NT-proBNP)

NT-proBNP has a central role in the regulation of blood pressure, blood volume, and sodium balance. Its levels increase with age, ventricular hypertrophy and in acute coronary syndromes, heart failure, and atrial fibrillation. NT-proBNP is considered a valuable predictor in diagnosis and prognosis of patients with symptoms of heart failure, left ventricular dysfunction, and acute coronary syndromes.

Indicate if the NT-proBNP is **Known** any time between diagnosis and the start of the preparative regimen / infusion. If **Known**, report the value report the value as documented on the laboratory report (in pg / mL) and the date the sample was collected. If the NT-proBNP was assessed multiple times, report the most recent results prior to the start of the preparative regimen / infusion. If NT-proBNP was not assessed or if no information is available to determine if NT-proBNP was assessed, report **Unknown**.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 40: Was an electrocardiogram performed?

An electrocardiogram (ECG or EKG) is a test that records the electrical activity of the heart, providing information about its rhythm and structure.

Indicate if an electrocardiogram was performed at any time between diagnosis and the start of the preparative regimen. If an electrocardiogram was not performed or if no information is available to determine if an electrocardiogram in this reporting period, report **No**.

WARRIOR-SCD

Attaching the report is required for WARRIOR-SCD.

Question 41: Indicate if the electrocardiogram report is attached

Indicate if the electrocardiogram was **Attached** in FormsNet3^{SM}. If multiple electrocardiograms were performed prior to the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

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For further instructions on how to attach documents in FormsNet3[SM], refer to the Training Guide.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q42 – 47: Renal Assessments

Questions 42 – 43: Blood pressure (BP)

Indicate if the recipient's blood pressure was measured prior to the start of the preparative regimen / infusion. If measured, select **Known** and provide the recipient's blood pressure. If blood pressure was measured on multiple times, report the most recent results prior to the start of the preparative regimen / infusion. If blood pressure was not measured or if no information is available to determine if blood pressure was measured, report **Unknown**.

Questions 44 – 45: Urine albumin

Indicate if urine albumin was measured any time between diagnosis and prior to the start of the preparative regimen / infusion. If measured, select **Known,** report the laboratory value and unit of measure documented on the laboratory report. If urine albumin was assessed on multiple times between diagnosis and prior the start of the preparative regimen / infusion, report the most recent results. If urine albumin was not measured or if no information is available to determine if urine albumin was measured prior the start of the preparative regimen / infusion, report **Unknown**.

If the urine albumin is < 0.1 mg / L, report the urine albumin value as "0 mg / L."

Questions 46 – 47: Urine creatine *(one time urine)*

Indicate if urine creatine was measured between diagnosis and prior to the start of the preparative regimen / infusion. This should be a *random urine creatine* not a *24-hour urine creatine*. If measured, select **Known,** report the laboratory value and unit of measure documented on the laboratory report. If urine creatine was assessed on multiple times prior to the start of the preparative regiment / infusion, report the most recent results. If urine creatine was not measured or if no information is available to determine if urine creatine was measured prior to the start of the preparative regiment / infusion, report **Unknown**.

Section Updates

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Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q48 – 52: Splenic Assessments

Question 48: Was splenic function assessed?

Evaluation of splenic tissue may be necessary to determine the extent of the recipient's disease. Splenic assessments include the following:

- **Complete RBC:** Also called an erythrocyte count, this assessment is used to determine how many red blood cells are present. One of the several tests included in a CBC.
- **Pitted RBC score:** As red blood cells (RBC) age, membrane vacuoles ("pits") occur. Pitted RBCs may be listed on laboratory reports as a "PIT count."
- **Splenic scan:** Radionuclide spleen scans (liver-spleen scans) are nuclear scan utilizing a radioactive tracer substance that is administered intravenously. The tracer collects in large amounts and shows as bright spots on imaging results. One of the most common methods used is single photon emission computed tomography (SPECT / CT).

Indicate **Yes** if splenic function was assessed by a complete RBC, pitted RBC score, or splenic scan at any time between diagnosis and the start of the preparative regimen / infusion.

If splenic function was not assessed or no information is available to determine if splenic function was assessed at any time between diagnosis and the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively. **Unknown** should be used sparingly.

Report **Not applicable** if the recipient had a prior splenectomy or was born without a spleen (congenital asplenia).

Questions 49 – 52: Select which splenic tests was completed

Indicate which splenic test (completed RBC, pitted RBC score, and/or splenic scan) was completed.

If a **Complete red blood cell count** was performed, specify the value and units of measurement as documented on the laboratory report.

If a **Pitted RBC score** was performed, specify the percentage.

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If a **Splenic scan** was performed, specify the results as either **Normal** *(radionuclide uptake)* or **Abnormal** *(no radionuclide uptake)*.

If any of the assessments were performed multiple times prior to the start of the preparative regimen / infusion, report the most recent results.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q53 – 57: Acute Chest Syndrome

Question 53: Has acute chest syndrome (ACS) occurred in the last two years?

Acute chest syndrome (ACS) is a term used to identify symptoms of chest pain, cough, fever, decreased oxygen (hypoxia), and lung infiltrates. Due to the sickling nature of red blood cells as a result of sickle cell disease, ACS may result in pulmonary infarction / emboli or viral / bacterial pneumonia. Diagnosis of ACS should be made based on clinical judgement.

Indicate if the recipient was clinically diagnosed with ACS in the last two years prior to the start of the preparative regimen / infusion. If diagnosed in the last two years, report **Yes**. If not clinically diagnosed or was diagnosed more than two years prior to the start of the preparative regimen / infusion, report **No**. If no information is available to determine if ACS was clinically diagnosed, report **Unknown**.

Questions 54 – 55: Total number of episodes within the last two years

Indicate if the total number of ACS episodes in the last two years prior to the start of the preparative regimen / infusion is **Known**. If **Known**, specify the number of episodes within the last two years. If the number of ACS episodes are not known, select **Unknown**.

In this context, an “episode” is defined as having clinical symptoms requiring intervention (i.e., antibiotics, steroids, etc.) followed by resolution of symptoms and discontinuation of intervention. This should not be interpreted as the number of days the recipient was receiving treatment or had active symptoms. An episode may also be referred to as an “event.”

Question 56: Were red blood cell transfusions required for treatment of ACS in the last two years? *(report any simple or exchanged transfusions prior to infusion)*

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Specify if red blood cell (RBC) transfusions were required to treat the ACS in the last two years prior to the start of the preparative regimen / infusion. Report **Yes** if RBC transfusion support was required to offset the clinical symptoms of ACS for any episode(s) within the last two years. This includes both simple and exchange transfusions. If RBC transfusions were not required in the last two years, report **No**. If no information is available to determine if RBC transfusion were required, report **Unknown**.

Question 57: Was intubation / mechanical ventilation required for treatment of ACS in the last two years?

A history of intubation and/or mechanical ventilation may impact the recipient's pulmonary function post-infusion.

Specify if intubation and / or mechanical ventilation was required to treat ACS in the last two years prior to the start of the preparative regimen / infusion. If the recipient was intubated and / or placed on mechanical ventilation due to ACS within the last two years, report **Yes**. If the recipient was not intubated and / or placed on mechanical ventilation within the last two years, report **No**. If no information is available to determine if the recipient was intubated and / or placed on mechanical ventilation, report **Unknown**.

Do not report **Yes** if the recipient uses a BIPAP or CPAP machine for sleep apnea.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q58 – 61: Pain

Question 58: Have vaso-occlusive pain episodes occurred that required hospitalization or treatment within the last 2 years? (*treatment that is in a hospital or clinic setting*)

Vaso-occlusive pain, sometimes called a pain crisis, is a common painful complication of sickle cell disease in adolescents and adults. Recurrent episodes may cause irreversible organ damage.

Specify if the recipient had vaso-occlusive pain episodes requiring treatment or hospitalization, such as ER admission, day hospital, inpatient admission, etc., in the last two years prior to the start of the

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preparative regimen. If the recipient did not experience vaso-occlusive pain requiring hospitalization or treatment, or if no information is available to determine if the recipient required hospitalization for vaso-occlusive pain in the past two years, report **No** or **Unknown**, respectively.

Questions 59 – 60: Total number of episodes in the last two years

Indicate if the number of vaso-occlusive pain episodes the recipient experienced in the last two years is **Known**. If **Known**, report the number of vaso-occlusive pain episodes requiring hospitalization or treatment within the past two years prior to the start of the preparative regimen. If the number of vaso-occlusive pain episodes requiring hospitalization or treatment is not known within the past two years, select **Unknown**.

In this context, an "episode" is defined as being admitted to a hospital setting (i.e., ER admission, day hospital, inpatient admission, etc.) followed by a discharge. This should not be interpreted as the number of days for which the recipient was hospitalized.

Question 61: Were opioids prescribed for the treatment of pain?

Opioids are typically listed in the medical administration record (MAR) and / or in the medication list documented on the progress note within the medical record. Examples of opioid treatment may include Morphine, Hydrocodone, Methadone, Hydromorphone (Dilaudid), etc.

Indicate if the recipient was prescribed opioids for treatment of either vaso-occlusive or chronic pain related to the primary disease for infusion during this reporting period. If opioids were prescribed for treatment of pain, either intravenous or oral, report **Yes**. If opioids were not prescribed for treatment of pain or if no information is available to determine if opioids were prescribed for treatment of pain, report **No**.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q62 – 69: Avascular Necrosis

Question 62: Has avascular necrosis occurred?

Avascular necrosis is the death of bone tissue due to a lack of adequate blood supply. It is sometimes called osteonecrosis and can lead to minute fractures in the bone followed by eventual

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collapse. Avascular necrosis can spread from joint to joint and commonly occurs in the hips and shoulders.

Indicate if avascular necrosis occurred at any time between diagnosis and the start of the preparative regimen / infusion. If avascular necrosis did not occur or no information is available to determine if avascular necrosis occurred at any time between diagnosis and the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Questions 63 – 64: Specify joint(s) affected *(check all that apply)*

Specify the joint(s) affected by avascular necrosis. If more than one joint was affected, select all that apply. If there was avascular necrosis of a joint not listed, report **Other** and specify the affected joint.

Question 65: Was a musculoskeletal MRI performed?

A musculoskeletal (MSK) MRI is a radiation-free imaging scan that uses a strong magnetic field and radio waves to create detailed pictures of bones, joints, muscles, tendons, ligaments, and soft tissues.

Indicate if a musculoskeletal MRI was performed at any time between diagnosis and the start of the preparative regimen / infusion. If musculoskeletal MRI was not performed or if no information is available to determine if a musculoskeletal MRI was performed prior to the start of the preparative regimen / infusion, report **No**.

WARRIOR-SCD

Attaching the report (when available) is required for WARRIOR-SCD.

Question 66: Indicate if the musculoskeletal MRI report is attached

Indicate if the musculoskeletal MRI was **Attached** in FormsNet3^{SM}. If multiple musculoskeletal MRIs were performed prior to the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 67 – 69: Did the recipient undergo joint replacement?

Osteonecrosis can lead to severe joint pain and early development of arthritis. Osteonecrosis is the most common reason for joint replacement in young recipients with sickle cell disease. This information should be under surgical history in the EMR.

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Specify if the recipient underwent joint replacement at any time between diagnosis and the start of the preparative regimen / infusion. If **Yes**, specify the location of the joint replacement. If more than one joint was replaced, select all that apply. If joint replacement took place in a location not listed, report **Other** and specify the replaced joint.

If joint replacement did not occur or no information is available to determine if joint replacement occurred at any time between diagnosis and the start of the preparative regimen / infusion, report **No**.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q70 – 79: Central Nervous System

Transcranial Doppler Velocity

This question applies to pediatric recipients 18 years old or younger only.

Questions 70 – 72: Was transcranial doppler velocity assessed? *(pediatric only)*

Transcranial doppler and transcranial color doppler are types of ultrasonography that measure the velocity of blood flow through the brain's blood vessels by measuring the echoes of ultrasound waves moving trans-cranially.

Indicate if transcranial doppler velocity was assessed at any time prior to the start of the preparative regimen. If **Yes**, report the date of the most recent assessment and the transcranial doppler velocity value in cm / sec

If transcranial doppler velocity was not assessed or if no information is available to determine if transcranial doppler velocity was assessed prior to the start of the preparative regimen, report **No** or **Unknown**, respectively.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Attaching Transcranial Doppler Velocity Report

This question is only applicable to WARRIOR-SCD

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WARRIOR-SCD

Attaching the report (when available) is required for WARRIOR-SCD.

Question 73: Indicate if the transcranial doppler velocity report is attached

Indicate if the transcranial doppler velocity was **Attached** in FormsNet3SM. If transcranial doppler velocity was assessed multiple times between diagnosis and prior to the start of the preparative regimen / infusion, attach the most recent report. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question 74: Was there a sickle cell central nervous system (CNS) complication?

A CNS complication is the development of different neurologic signs and symptoms that occur in recipients with sickle cell disease. See *Specify type of CNS complication* below for a list of CNS events.

Specify if the recipient experienced a sickle cell CNS event at any time between diagnosis and the start of the preparative regimen / infusion. If a sickle cell CNS event did not occur or no information is available to determine if a CNS event occurred prior to the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Reporting Multiple Sickle Cell CNS Events

Complete *Specify type of CNS complication, Year of onset,* and *Was an MRI / MRA of the brain performed for the diagnosis of this reported CNS complication?* for each sickle cell CNS complication in the reporting period by adding an additional instance in the FormsNet3SM application.

Question 75: Specify type of CNS complication

Indicate the type of sickle cell CNS event that occurred. If multiple sickle cell CNS complications occurred, report each sickle CNS complication as a separate instance. If the same sickle cell CNS complication occurred multiple times throughout the reporting period (e.g. multiple seizures), only one instance needs to be reported.

- **Cerebral venous thrombosis**: A blood clot in the cerebral vein in the brain.
- **Hemorrhagic stroke**: Blood vessels break and bleeds in the brain.
- **Ischemic stroke**: The most common type of stroke. Occurs when a blood vessel in the brain is blocked or narrowed, causing reduced blood flow.
- **Moyamoya**: A rare condition where the carotid artery is blocked or narrowed which reduces the blood flow to the brain.

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- **Overt stroke**: A focal neurological deficit lasting more than 24 hours. If the type of CNS event is not documented and only noted as a "stroke," select this option.
- **Posterior reversible encephalopathy syndrome (PRES)**: An acute neurotoxic syndrome that is characterized by a spectrum neurological and radiological feature from various risk factors. Common neurological symptoms includes headache, impairment in level of consciousness, seizures, visual disturbances, and focal neurological deficits
- **Seizure**: Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minors physical sings, thought disturbances or a combination of symptoms.
- **Silent stroke**: Asymptomatic stroke, usually found on a screening brain MRI. Often associated with cognitive deficits.
- **Transient ischemic stroke**: A temporary period of mild stroke symptoms that lasts only a few minutes and does not result in permanent damage. This is also known as transient ischemic attack or a ministroke.

Questions 76 – 77: Year of onset

Indicate if the year of onset of the CNS event being reported in this instance is **Known**. If **Known**, report the year of onset.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 78: Was an MRI / MRA of the brain performed for the diagnosis of this reported CNS event?

Magnetic resonance imaging (MRI) is an imaging technique used to form pictures of the anatomy and the physiological processes of the body. Magnetic resonance angiography (MRA) is similar to MRI but is used to specifically examine blood vessels.

Indicate if an MRI or MRA of the brain was performed to diagnose the CNS event being reported in this instance.

If an MRI / MRA of the brain was not performed to diagnose the CNS event being reported in this instance or if no information is available to determine if an MRI / MRA of the brain was performed to diagnose the CNS event being reported in this instance, report **No** or **Unknown**, respectively.

WARRIOR-SCD

Attaching the report (when available) is required for WARRIOR-SCD.

Question 79: Indicate if the MRI / MRA report is attached

Indicate if the MRI / MRA report performed to diagnose the CNS event being reported in this instance was **Attached** in FormsNet3^{SM} . The diagnostic MRI / MRA report may not be the most

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recent scan performed prior to the start of the preparative regimen / infusion. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q80 – 90: Other Symptoms

Priapism

Questions regarding priapism are applicable to only biologically male recipients.

Question 80: Did one or more episodes of priapism occur? *(to be answered for males only)*

Priapism is defined as prolonged erection of the penis, usually without sexual arousal.

Indicate if the recipient experienced one or more episodes of priapism (with or without treatment) at any time between diagnosis and the start of the preparative regimen. If the recipient did not experience priapism or no information is available to determine if the recipient experienced priapism, report **No** or **Unknown**, respectively.

Question 81: Was surgery performed at any time to correct blood flow?

If the recipient experienced an episode(s) of priapism, indicate if surgery was required at any time to correct the blood flow. If surgery was not performed or if no information is available to determine if surgery was performed to correct blood flow as a result of priapism prior to the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Question 82: Has sickle cell retinopathy developed?

Sickle cell retinopathy is an ocular manifestation of sickle cell disorders characterized by ocular damage due to trapping of sickle-shaped cells in the small blood vessels of the eye. Diagnosis of sickle cell retinopathy should be made by an ophthalmologist and is typically documented within the recipient's medical record.

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Indicate if the recipient developed sickle cell retinopathy at any time between diagnosis and the start of the preparative regimen / infusion. If the recipient did not develop sickle cell retinopathy or if no information is available to determine if the developed sickle cell retinopathy prior the start of the preparative regimen / infusion., report **No** or **Unknown**, respectively. The **Unknown** option should be selected sparingly and only when no information is available to determine if sickle cell retinopathy was diagnosed.

Question 83: Have chronic leg ulcers developed?

Chronic leg ulcers are defined as a defect of the skin below the level of the knee persisting for more than six weeks with no tendency to heal after three or more months.

Indicate whether the recipient developed chronic leg ulcers at any time between diagnosis and the start of the preparative regimen / infusion. If chronic leg ulcers did not develop or if no information is available to determine if chronic leg ulcers developed prior to the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Question 84: Is there a diagnosis of asthma or a reactive airway disease?

Asthma is a condition where the airways narrow, swell, and produce extra mucus which results in breathing difficulty, coughing, wheezing, and shortness of breath. Reactive airway disease (RAD) is a general term used to describe coughing, wheezing or shortness of breath when a specific diagnosis has not been made (i.e., asthma, chronic obstructive pulmonary disease, etc.).

Indicate if there was a diagnosis of asthma or a reactive airway disease between diagnosis and the start of the preparative regimen / infusion. If the recipient was not diagnosed with or if no information is available to determine if there was a diagnosis of asthma or reactive airway disease prior to the start of the preparative regimen / infusion, report **No** or **Unknown**, respectively.

Question 85: Has a venous thromboembolism developed?

Venous thrombosis embolism, also called a venous thromboembolism, is a condition characterized by formation of blood clots in deep veins of the body. These clots typically manifest in the lower leg, thigh, or pelvis, but have been noted to occur in the arm.

Indicate if the recipient developed a venous thromboembolism between diagnosis and the start of the preparative regimen / infusion. If a venous thromboembolism did not develop or if no information is available to determine if a venous thrombosis embolism developed prior to the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

Question 86: Was it associated with an indwelling catheter?

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There are several types of long-term indwelling central line catheters used to access veins. Examples include Hickman, Broviac, PICC, etc. which carry a risk of developing a blood clot.

Indicate if the venous thromboembolism was associated with the recipient's indwelling catheter. If the venous thromboembolism was not associated with the recipient's indwelling catheter or if no information is available to determine if the venous thromboembolism was associated with the recipient's indwelling catheter prior to the start of the preparative regimen / infusion, report **No**.

Question 87: Has a pulmonary embolism developed?

Pulmonary embolism is a medical condition where a blood clot is lodged in an artery of the lung, blocking blood flow to that area.

Indicate if the recipient developed a pulmonary embolism between diagnosis and the start of the preparative regimen / infusion. If a pulmonary embolism did not develop or if no information is available to determine if a pulmonary embolism developed prior to the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

Question 88: Was it associated with an indwelling catheter?

There are several types of long term indwelling central line catheters used to access veins. Examples include Hickman, Broviac, PICC, etc. which carry a risk of developing a blood clot.

Indicate if the pulmonary embolism was associated with the recipient's indwelling (central line) catheter. If the pulmonary embolism was not associated with the recipient's indwelling catheter or if no information is available to determine if the pulmonary embolism was associated with the recipient's indwelling catheter prior to the start of the preparative regimen / infusion, report No.

Red box: does not apply if spleen has been removed
Dfsdf

Question 89: Number of splenic sequestration events

The diagnosis of a splenic sequestration crisis is usually clinical, using recipient history, physical exam, and accompanying lab values. This typically requires seeking medical care for urgent diagnosis and management. An event is defined as the documentation of this diagnosis after seeking medical care either in clinic, emergency department, or hospitalization.

Specify the number of splenic sequestration events prior to the start of the preparative regimen / infusion.

Question 90: Date of last event

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Report the date of the last splenic sequestration event requiring hospitalization or treatment prior to the start of the preparative regimen / infusion. This is typically documented within the progress notes.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q91 -102: Existing Organ Impairments

Multiple Organ Impairments

Complete *Specify co-existing diseases or organ impairments any time prior to start of preparative regimen, Date of diagnosis, Method used to assess osteopathies, DEXA scan vertebral, DEXA scan hip, Quantitative CT vertebral* and *Quantitative CT vertebral* for each organ impairment in the reporting period by adding an additional instance in the FormsNet3^{SM} application.

Question 91: Specify co-existing diseases or organ impairments any time prior to start of preparative regimen

Indicate if the recipient developed any of the co-existing diseases or organ impairments listed below at any time between diagnosis and prior to the start of the preparative regimen / infusion. Include any impairments that were resolved prior to the preparative regimen and did not recur.

- **Amenorrhea:** Absence of menstruation
- **Cardiomyopathy:** A disease of the heart muscle that makes it more difficult for the heart to pump blood to the rest of the body
- *Cholelithiasis: Presence of one or more gallstones in the gallbladder
- **Growth hormone deficiency / short stature:** A condition in which the body does not produce enough growth hormone / a reduced overall rate of growth.
- **Hypersplenism:** Overactive spleen. Diagnosis is typically based on a physician's exam (checking for splenomegaly), a CBC to assess the concentration of red and white blood cells, and / or an ultrasound, measuring the size of the spleen.

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- **Hypogonadism / Gonadal dysfunction:** A condition where there is a hyperfunction of the gonads. It can manifest as precocious puberty and is caused by abnormally high levels of testosterone or estrogen, crucial hormones for sexual development.
- **Hypothyroidism requiring replacement therapy:** Decreased activity of the thyroid gland. Diagnosis of hypothyroidism includes high levels of thyroid-stimulating hormone (TSH). Symptoms of hypothyroidism include fatigue, depression, weakness, weight gain, musculoskeletal pain, decreased taste, hoarseness, and / or puffy face.
- **Osteonecrosis:** Flow to part of a bone is disrupted. This results in death of bone tissue, and the bone can eventually break down and the joint will collapse.
- **Osteopathies (porosis, penia):** Includes osteoporosis or osteopenia. Osteopathies should be reported if osteopenia or osteoporosis is documented within the medical record by the physician or based on the Z or T-score. Osteopenia is defined as a Z or T-score between -1.0 and -2.0 by a DEXA or quantitative CT scan. Osteoporosis is defined as a Z or T-score less than -2.0 by a DEXA or quantitative CT scan.
- **Pulmonary hypertension:** Refers to elevated pulmonary arterial pressure and is diagnosed either by an echocardiogram or right heart catheterization.
- **Retinal changes:** Changes include but are not limited to macular degeneration, floaters, diabetic eye disease, retinal detachment, and retinitis pigmentosa.
- **Thrombosis:** Blood clot within the vein or artery.

If the recipient did not develop any of the co-existing diseases or organ impairments listed above at any time prior to the start of the preparative regimen, select **None**.

Question 92: Date of diagnosis

Report the diagnosis date of the co-existing disease or organ impairment. If the organ impairment occurred multiple times prior to the start of the preparative regimen / infusion, report the co-existing disease or organ impairment once and the diagnosis date of the most recent occurrence. See the example below for additional information.

If the exact date is not known report an estimated date and check the **Date estimated** box.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

- **Example 1:** A recipient developed a blood clot (thrombosis) on 1/15/2018 which resolved; however, the recipient developed another blood clot 8/20/2023. The recipient's transplant was on 12/1/2023. The diagnosis date of the thrombosis should be reported as 8/20/2023 as this is the date of the most recent episode.

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Question 93: Method used to assess osteopathies (*report the most recent Z or T-score available. Z-scores are used in patients younger than or equal to 20 and T-scores in patients older than 20*) *(check all that apply)*

Specify the method used to assess the osteopathy being reporting in this instance. Select all that apply.

If the method was not documented or if no information is available to determine the method, report **Unknown**.

Questions 94 – 95: DEXA scan vertebral

Indicate if the vertebral Z-score by DEXA is **Known**. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).

If multiple DEXA scans were performed between diagnosis and the start of the preparative regimen / infusion, report the most recent vertebral Z or T-score.

Questions 96 – 97: DEXA scan hip

Indicate if the hip Z-score by DEXA is **Known**. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).

If multiple DEXA scans were performed between diagnosis and the start of the preparative regimen / infusion,, report the most recent hip Z or T-score

Questions 98 – 99: Quantitative CT vertebral

Indicate if the vertebral Z-score by quantitative CT is **Known**. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).

If multiple quantitative CT scans were performed between diagnosis and the start of the preparative regimen / infusion, report the most recent vertebral Z or T-score.

Questions 100 – 101 : Quantitative CT hip

Indicate if the hip Z-score by quantitative CT is **Known**. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).

If multiple quantitative CT scans were performed between diagnosis and the start of the preparative regimen / infusion, report the most recent hip Z or T-score.

DEXA Scan report

This question is only applicable to WARRIOR-SCD

WARRIOR-SCD

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Attaching the report (when available) is required for WARRIOR-SCD.

Questions 102: Indicate if the DEXA scan report is attached

Indicate if the DEXA scan was **Attached** in FormsNet3^{SM}. If multiple DEXA scans were performed, attach the most recent report prior to the start of the preparative regimen / infusion. Attaching the report will prevent future requests to submit additional data for research studies.

If the report is not available for any reason, select **Not available**.

For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q103 – 104: Infection

Questions 103: Does the recipient have a history of clinically significant bacterial bloodstream infection? *(any prior clinically significant infection, e.g., sepsis)*

Bloodstream infections (BSI) are a common cause of morbidity and mortality in people with sickle cell disease (SCD). In children with SCD, BSI are most often caused by encapsulated organisms. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Indicate if the recipient has a history of clinically significant bacterial BSI at any time prior to the start of the preparative regimen / infusion. If unknown, select **No**.

If the recipient does not have a history of clinically significant BSI or if no information is available to determine if the recipient has a history of clinically significant BSI prior to the start of preparative regimen / infusion, report **No**.

Question 104: Does the recipient have a history of clinically significant bacterial bone infection? *(any prior clinically significant infection, e.g., osteomyelitis)*

Recipients with SCD are at an increased risk for orthopedic manifestations such as osteomyelitis. Usually, osteomyelitis affects the diaphysis of long bones, such as the femur and humerus, but it is possible for any other bone to be affected. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Indicate if the recipient has a

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history of clinically significant bacterial bone infection at any time prior to the start of the preparative regimen / infusion.

If the recipient does not have a history of clinically significant bacterial bone infections or if no information is available to determine if the recipient has a history of clinically significant bacterial bone infections prior to the start of preparative regimen / infusion, report **No**.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q 105 – 111: Disease Modifying Therapies

Question 105: Were disease modifying therapies given? (*excludes blood transfusions*)

Indicate if the recipient received disease modifying therapies at any time between diagnosis and the start of the preparative regimen / infusion; excluding blood transfusion(s). See the question below for a list of common disease modifying therapies.

If the recipient did not receive disease modifying therapies or if no information is available to determine if the recipient received disease modifying therapies, select **No** or **Unknown**, respectively.

Disease Modifying Therapies

Complete questions *Specify the disease modifying therapy, Date therapy started, Date therapy stopped* for each disease modifying therapy received in the reporting period by adding an additional instance in the FormsNet3^{SM} application.

Same Therapy Restarted

If the same therapy was started and stopped multiple times prior to the start of the preparative regimen, only one instance needs to be reported. In this case, report the therapy start date as the date when therapy first began.

Questions 106 – 107: Specify the disease modifying therapy

Select the disease modifying therapy the recipient received. If the recipient received a therapy which is not listed, select **Other** and specify the treatment. Report the generic name of the agent, not the brand name.

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- **Crizanlizumab (Adakveo)**: A monoclonal antibody given to reduce the frequency of vaso-occlusive crises.
- **Hydroxyurea**: A type of chemotherapy. Common brand names include Droxia, Hydrea, Xromi.
- **L-Glutamine (Endari)**: An amino acid in the form of an oral powder given to reduce the complications of sickle cell disease.
- **Voxelotor (Oxbryta)**: An oral medication given to inhibit sickle hemoglobin polymerization.

Questions 108 – 109: Date therapy started

Indicate whether the therapy start date is **Known**. If **Known**, report the date the recipient began this line of therapy. If the exact date is not known report an estimated date and check the **Date estimated** box.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 110 – 111: Date therapy stopped

Indicate if the stop date is **Known**. If **Known**, use the following guidelines when reporting the end date:

- If the therapy is administered in cycles (i.e., Crizanlizumab), report the date the recipient started the last cycle for this line of therapy.
- If the therapy is administered on a daily basis, report the last date the recipient received the line of therapy being reported.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Report **Not applicable** if the recipient is still receiving therapy at the start of the preparative regimen / infusion.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q112 – 137: Other Laboratory Studies

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Questions 112 – 113: Was hemoglobin electrophoresis performed? *(do not include results if an RBC transfusion occurred within 4 weeks of the electrophoresis study)*

Indicate if hemoglobin electrophoresis studies were performed between diagnosis and the start of the preparative regimen / infusion. If **Yes,** provide the date of the *most recent* hemoglobin electrophoresis study performed prior to the start of the preparative regimen / infusion.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

If hemoglobin electrophoresis studies were not performed or if no information is available to determine if hemoglobin electrophoresis studies were performed between diagnosis and the start of the preparative regimen or infusion, report **No** or **Unknown**, respectively.

If RBC transfusion(s) were given within four weeks of the hemoglobin electrophoresis, report **Not applicable**.

Hemoglobin Electrophoresis

Some centers do not routinely perform hemoglobin electrophoresis studies and may perform chimerism studies instead. The chimerism results are reported in the Chimerism Studies section of the Post-Infusion Follow-Up (2100) Form. For centers that performed both hemoglobin electrophoresis and chimerism studies, report the results of both on the appropriate forms.

Hemoglobin Types: Hb A and Hb A1

Hb A and Hb A1 are the same hemoglobin types. If Hb A1 is assessed, report these results under **Hb A.**

Questions 114 – 126: Specify the hemoglobin allele types based on the sample tested

Specify the hemoglobin allele types identified in the hemoglobin electrophoresis study reported above. If the hemoglobin allele type was identified, report **Yes** and specify the percentage. If additional sickle related hemoglobin allele types are identified and not listed as options on the form, report **Yes** for *Other sickle related hemoglobin allele type*, specify the other hemoglobin allele type, and provide the percentage.

Report **No** if the specified hemoglobin allele type was not assessed in the hemoglobin electrophoresis study reported above.

Questions 127 – 129: Were absolute reticulocyte counts tested?

Indicate if absolute reticulocyte counts were assessed between diagnosis and the start of the preparative regimen / infusion. If **Yes**, provide the absolute reticulocyte cell count, the unit of measurement as noted on the laboratory report, and specify date the sample was collected for

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examination. If the absolute reticulocyte count was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If absolute reticulocyte counts were not tested or if no information is available to determine if absolute reticulocyte counts were tested between diagnosis and the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 130 – 132 Were soluble transferrin receptors (sTfR) tested?

Soluble transferrin receptors (sTfR) are proteins found in the blood and used as a measure of functional iron status. These levels are typically elevated in individuals with an iron deficiency (i.e., iron deficiency anemia). This assessment is a blood test and may be performed at the transplant center or by an outside facility.

Indicate if sTfR was tested prior to the start of the preparative regimen / infusion. If **Yes**, provide the sTfR value in mg / L, and specify the date the sample was collected for examination. If the sTfR was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If the sTfR was not tested or if no information is available to determine if sTfR was tested prior the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 133 – 135: Was an erythropoietin (EPO) level tested ?

Erythropoietin (EPO) is a hormone predominantly produced in the kidneys which plays a critical role in the production of red blood cells.

Indicate if an EPO level was obtained prior to the start of the preparative regimen / infusion. If **Yes**, provide the EPO level in IU / L, and report the date the sample was collected for examination. If the EPO was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If EPO levels were not tested or if no information is available to determine if EPO levels were test prior to the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Questions 136 – 137: Was a D-dimer level tested?

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D-dimer is a byproduct of the blood clotting and breakdown process, serving as a marker of ongoing coagulation and fibrinolysis. The D-Dimer test is a quantitative immunoturbidimetric test, elevated levels may indicate the presence of pulmonary embolism, deep vein thrombosis, arterial thrombosis or DIC.

Indicate if a D-Dimer test was conducted prior to the start of the preparative regimen / infusion. If **Yes**, provide the D-dimer level and the units of measurement as noted on the laboratory report. If the D-dimer test was taken multiple times, report the value and date of the most recent assessment prior to the start of the preparative regimen / infusion.

If D-dimer tests were not measured or if no information is available to determine if D-dimer tests were conducted prior to the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q138 – 139: Reason for Infusion

Questions 138 – 139: What was the primary reason for infusion?

Specify the recipient's *primary* reason for the infusion. If the indication for infusion is not listed, select **Other** and specify the reason.

If there are multiple indications for which the recipient is receiving the infusion, confirm with the physician the primary reason; only one indication may be reported.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

Q140: Marrow Evaluation at Last Evaluation

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Marrow Evaluation

Complete Was a marrow aspirate and / or biopsy performed? for gene therapy infusions only.

Questions 140: Was a marrow aspirate and / or biopsy performed?

Indicate if a marrow aspirate and or biopsy was performed prior to the start of the preparative regimen / infusion.

If the recipient is enrolled in WARRIOR-SCD, also complete the Laboratory Studies (3502) Form and Marrow Surveillance (3506) Form. The intent is to screen for and / or identify changes in the marrow such as dysplasia, MDS, or new hematologic malignancy

Report **Unknown** if there is no information to determine if a marrow aspirate or biopsy was completed at any time prior to the preparative regimen / infusion.

Section Updates

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (if applicable)

DRAFT

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