PRIOR AUTHORIZATION POLICY

POLICY: Hematology – Gene Therapy – Casgevy Prior Authorization Policy
- Casgevy™ (exagamglogene autotemcel intravenous infusion – Vertex/CRISPR Therapeutics)

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OVERVIEW

Casgevy, an autologous hematopoietic stem cell-based gene therapy, is indicated for the following uses:[1]
- **Sickle cell disease** in patients ≥ 12 years of age with recurrent vaso-occlusive crises (VOCs).
- **Transfusion-dependent beta-thalassemia** (TDT) in patients ≥ 12 years of age.

Casgevy is given one-time (per lifetime) as a single dose, which contains a minimum of 3×10^6 cluster of differentiation 34+ (CD34+) cells/kg of body weight. Casgevy is given as an intravenous (IV) infusion. The manufacturing time (which includes quality control) for Casgevy can take up to 6 months. However, the entire process can take 8 months or longer as patients need to undergo mobilization and apheresis procedures and myeloablative conditioning prior to Casgevy infusion.

Casgevy is prepared from the patient's own hematopoietic stem cells, which are obtained via apheresis procedure(s).[1,2] The CD34+ cells collected from the patient are modified *ex-vivo* by highly specific clustered, regularly interspaced, short palindromic repeats (CRISPR) and CRISPR-associated protein 9 nucleases (CRISPR/Cas9)-mediated gene editing. CRISPR/Cas9 specifically edits the B-cell lymphoma/leukemia 11A (BCL11A) gene. After Casgevy infusion, the edited CD34+ cells engraft in the bone marrow and differentiate to erythroid lineage cells with reduced BCL11A expression. Downregulation of BCL11A expression in the erythroid progenitors of the bone marrow results in reduced BCL11A protein levels, which leads to an increase in γ-globin expression and increased fetal hemoglobin (HbF) production. In patients with TDT, γ-globin production improves the α-globin to non α-globin imbalance, thereby reducing ineffective erythropoiesis and hemolysis and increasing total hemoglobin (Hb) levels, which eliminates the dependence on regular red blood cell (RBC) transfusions. In patients with sickle cell disease, increased HbF levels (≥ 20%) are protective against disease complications, including preventing VOCs.[2]

Disease Overview

Sickle Cell Disease

Sickle cell disease is a group of inherited RBC disorders characterized by the presence of a mutated Hb subunit beta gene.[3-5] Healthy RBCs are round and contain Hb. In contrast, in a patient with sickle cell disease, RBCs are sickle-shaped and die early, resulting in a constant shortage of RBCs. Furthermore, the sickle-shaped RBCs aggregate in the bloodstream, causing vaso-occlusion, which deprive downstream tissues of nutrients and oxygen, resulting in tissue ischemia, organ damage, and hemolysis (which leads to anemia). In the US, approximately 100,000 persons have the condition and it is estimated 20,000 patients have severe sickle cell disease.[2,3]

Patients with severe sickle cell disease have one of the following genotypes: β^S/β^S, β^S/β^0, β^S/β^+.[2-5] These patients have recurrent VOCs/vaso-occlusive events, while receiving appropriate supportive care (e.g., pain management, hydroxyurea). Management of sickle cell disease focuses on preventing and treating pain episodes and other complications; symptomatic treatment includes use of analgesics, fluids (hydration), oxygen supplementation, and blood transfusion. Allogeneic hematopoietic stem cell transplantation

(HSCT), a potentially curative therapy, requires a stem cell donor, typically a human leukocyte antigen (HLA)-matched donor; less than 20% of patients with sickle cell disease have a suitable donor.[2] Pharmacologic treatments for sickle cell disease include Adakveo® (crizanlizumab-tmca IV infusion), Endari® (L-glutamine oral powder), hydroxyurea, and Oxbryta® (voxelotor tablets and tablets for oral suspension).[6-10]

Transfusion-Dependent Beta-Thalassemia

The condition of beta-thalassemia is a group of recessively inherited blood disorders caused by beta-globin gene mutations that either reflect a reduced (β^+) or relative lack (β^0) of production of functional beta-globin.[11] The attenuated or lack of Hb results in chronic anemia of varying degrees of severity and insufficient delivery of oxygen to the body. Those with severe anemia may require lifelong RBC transfusions and regular iron chelation to prevent iron overload. The extremely low Hb levels can lead to many types of symptoms and health-related issues (e.g., dizziness, weakness, fatigue, increased cardiac effort, tachycardia, poor growth) or ineffective erythropoiesis (e.g., bone changes, massive splenomegaly). An estimated 3,000 persons in the US have beta-thalassemia and slightly less than one-half of the patients are dependent on RBC transfusions.

Clinical Efficacy

Sickle Cell Disease

Casgevy is being evaluated in an ongoing, single-dose, multicenter study involving adolescents and adults with sickle cell disease.[1,2] Eligible patients underwent mobilization and apheresis procedures to collect CD34+ stem cells for Casgevy manufacturing, followed by myeloablative conditioning with busulfan and infusion of Casgevy. All of the enrolled patients had one of the following genotypes: β^S/β^S, β^S/β^0, or β^S/β^+. In addition, all patients had severe sickle cell disease, as defined by the occurrence of at least two of the following VOC events per year during the 2-year period before screening, while receiving appropriate supportive care: acute pain that required a visit to a medical facility and administration of pain medications (opioids or IV nonsteroidal anti-inflammatory drugs) or RBC transfusions; acute chest syndrome; priapism lasting more than 2 hours and requiring a visit to a medical facility; or splenic sequestration. Key exclusion criteria were patients with the following: clinically significant and active bacterial, viral, fungal, or parasitic infection; advanced liver disease; history or presence of Moyamoya disease; and prior or current malignancy or myeloproliferative disorder or significant immunodeficiency disorder. The primary efficacy set (PES) [n = 31] was composed of patients who received Casgevy infusion and were followed for at least 16 months after infusion.[1] At the interim analysis (June 2023 cut-off date), the median age of patients in the PES was 21 years; 23% of patients were adolescents (≥ 12 and < 18 years of age). At baseline, the annualized (median) rate of severe VOCs during the previous 2 years was 3.5 and the annualized (median) rate of hospitalizations due to severe VOCs during the previous 2 years was 2.0. All patients received plerixafor for mobilization and busulfan for myeloablative conditioning. Casgevy was administered as an IV infusion. The primary efficacy endpoint was the proportion of patients who did not experience a severe VOC for at least 12 consecutive months within the first 24 months after Casgevy infusion (VF12 responders) and the key secondary endpoint was the proportion of patients who did not require hospitalization due to severe VOCs for at least 12 consecutive months within the first 24 months after Casgevy infusion (HF12 responders). Evaluation of both endpoints began 60 days after the last RBC transfusion for post-transplant support or sickle cell disease support. The VF12 response rate was 93.5% (n = 29/31) and all 30 patients evaluable for HF12 response achieved this endpoint.

Transfusion-Dependent Beta-Thalassemia

Casgevy is being studied in an ongoing, open-label, multicenter, single-arm study involving adolescents and adults with TDT.[1] Eligible patients underwent mobilization and apheresis procedures to collect CD34+ stem cells for Casgevy manufacturing, followed by myeloablative conditioning and Casgevy infusion. Patients were followed for 24 months after Casgevy infusion. All of the enrolled patients had a history of requiring transfusions of 100 mL/kg/year or more of packed RBCs in the 2 years prior to enrollment or requiring at least 10 units/year of packed RBCs in the 2 years prior to enrollment. In addition, patients had one of the following genotypes for beta-thalassemia: β^0/β^0-like (including β0/β+[IVS-I-110] and β+[IVS-I-110]/β+[IVS-I-110]) and non-β^0/β^0-like. The PES [n = 35] was composed of patients who received Casgevy infusion and had adequate follow-up for evaluation of the primary efficacy endpoint. At the interim analysis (conducted based on January 2023 data cut-off), the median age of the patients was 20 years; 31.4% of the patients were adolescents (≥ 12 and < 18 years of age). At baseline, the annualized (median) RBC transfusion volume was 205 mL/kg and the annualized (median) number of RBC transfusion episodes was 17. All of the patients received a granulocyte-colony stimulating factor (G-CSF) and plerixafor to mobilize stem cells for apheresis and busulfan for myeloablative conditioning. Casgevy (median dose of 7.5×10^6 cells/kg) was administered as an IV infusion. At the interim analysis, the median (minimum, maximum) duration of follow-up was 23.8 (16.1, 48.1) months after Casgevy infusion. The primary efficacy endpoint was the proportion of patients achieving transfusion independence for at least 12 consecutive months (TI12), which was defined as maintaining weighted average Hb ≥ 9 g/dL without RBC transfusions for at least 12 consecutive months, within the first 24 months after Casgevy infusion. Evaluation of this endpoint started 60 days after the last RBC transfusion for post-transplant support or TDT disease management. In total, 32 of 35 patients achieved TI12; the responder rate was 91.4% (98.3% one-sided confidence interval [CI]: 75.7%, 100%). All of the patients who achieved TI12 remained transfusion-independent, with a median duration of 20.8 months and normal mean weighted average total Hb levels of 13.1 g/dL. The median time to last RBC transfusion for patients who achieved TI12 was 30 days after Casgevy infusion. The three patients who did not achieve TI12 had reductions in annualized RBC transfusion volume requirements of 79.8%, 83.9%, and 97.9%, respectively, compared to baseline requirements. In addition, the three patients had reductions in annualized transfusion frequency of 78.6%, 67.4%, and 94.6%, respectively, compared to baseline requirements.

Guidelines

Sickle Cell Disease

Sickle cell disease guidelines have not incorporated gene therapies following their FDA approval. The American Society of Hematology (ASH) released evidence-based recommendations for stem cell transplantation for patients with sickle cell disease in 2021.[12] ASH notes that it is unclear how gene therapies will affect sickle cell disease outcomes, including organ complications and if broader access to curative therapy will alter the trajectory of sickle cell disease outcomes. ASH notes that while success rates after allogeneic HSCT are increasing, survival rates in patients receiving disease-modifying medications (e.g., hydroxyurea, L-glutamine, Adakveo, Oxbryta) and supportive care are also improving. More than 90% of patients who have undergone HSCT (predominantly using HLA-identical family donors) have been cured of sickle cell disease, as reported in short-term follow-up. Allogeneic HSCT is an established therapeutic option for patients with sickle cell disease with a clinical indication and an HLA-identical family donor. However, for the majority of patients, there are no suitable donors.

Transfusion-Dependent Beta-Thalassemia

Guidelines have not addressed Casgevy. In 2021, the Thalassaemia International Federation published guidelines for the management of TDT.[13]

- **Chelation therapy** was cited as an effective treatment modality in improving survival, decreasing the risk of heart failure, and decreasing morbidities from transfusion-induced iron overload. The

optimal chelation regimen should be individualized and will vary among patients and their clinical status.

- **Allogeneic hematopoietic stem cell transplant (HSCT)** should be offered to patients with beta-thalassemia at an early age, before complications due to iron overload have developed if an HLA-identical sibling is available. In some clinical circumstances, a matched unrelated donor can be adequate.
- **Reblozyl®** (luspatercept-aamt subcutaneous injection), an erythroid maturation agent, can be considered for patients ≥ 18 years of age who require regular RBC transfusions.
- **Zynteglo™** (betibeglogene autotemcel intravenous infusion), when available, may be an option for selected patients. Examples include young patients (12 to 17 years of age) with a β^+ genotype who do not have an HLA-compatible sibling donor. Also, Zynteglo can be considered in patients 17 to 55 years of age with a β+ genotype who do not have severe comorbidities and are at risk or ineligible to undergo allogeneic HSCT but can otherwise undergo an autologous gene therapy procedure with an acceptable risk.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Casgevy. Approval is recommended for those who meet the Criteria for the listed indications.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Casgevy as well as the specialized training required for administration of Casgevy, approval requires Casgevy to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) as a single dose. The approval duration is 1 year to allow for an adequate timeframe to prepare and administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. In the criteria for Casgevy, as appropriate, the symbol (†) is noted next to the specified gender. In this context, the specified gender is defined as follows: females/males are defined as individuals with the biological traits of a woman/man, regardless of the individual's gender identity or gender expression.

All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with eviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@eviCore.com prior to completing the review.

Documentation: Documentation is required for use of Casgevy as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Casgevy is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Sickle Cell Disease.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, N, and O):
   - **A)** Patient is ≥ 12 years of age; AND
   - **B)** Patient has not received a gene therapy for sickle cell disease in the past **[verification in claims history required]**; AND
     Note: If no claim for Casgevy or Lyfgenia (lovotibeglogene autotemcel intravenous infusion) is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Casgevy or Lyfgenia.
   - **C)** According to the prescribing physician, a hematopoietic stem cell transplantation is appropriate for the patient; AND
   - **D)** Patient meets ONE of the following (i or ii):
     - **i.** Patient does not have a Human Leukocyte Antigen (HLA)-matched donor; OR
     - **ii.** Patient has an HLA-matched donor, but the individual is not able or is not willing to donate; AND
   - **E)** Genetic testing **[documentation required]** indicates the patient has ONE of the following sickle cell disease genotypes (i, ii, or iii):
     - **i.** β^S/β^S genotype; OR
     - **ii.** β^S/β^0 genotype; OR
     - **iii.** β^S/β^+ genotype; AND

     Note: Other genotypes will be reviewed by the Medical Director on a case-by-case basis.
   - **F)** Patient has tried at least ONE pharmacologic treatment for sickle cell disease **[documentation required]**; AND
     Note: Examples of pharmacologic treatment for sickle cell disease include hydroxyurea, L-glutamine, Adakveo (crizanlizumab-tmca intravenous infusion), and Oxbryta (voxelotor tablets and tablets for oral suspension).
   - **G)** While receiving appropriate standard treatment for sickle cell disease, patient had at least four severe vaso-occlusive crises or events in the previous 2 years, as defined by the following (i, ii, iii, iv, or v):
     - **i.** An episode of acute pain that resulted in a visit to a medical facility which required administration of at least ONE of the following (a or b) **[documentation required]**:
       - **a)** Intravenous opioid; OR
       - **b)** Intravenous nonsteroidal anti-inflammatory drug; OR
     - **ii.** Acute chest syndrome **[documentation required]**; OR
       Note: Acute chest syndrome is defined by the presence of a new pulmonary infiltrate associated with pneumonia-like symptoms (e.g., chest pain, fever [> 99.5°F], tachypnea, wheezing or cough, or findings upon lung auscultation).
     - **iii.** Acute hepatic sequestration **[documentation required]**; OR
       Note: Acute hepatic sequestration is defined by a sudden increase in liver size associated with pain in the right upper quadrant, abnormal results of liver function test not due to biliary tract disease, and the reduction of hemoglobin concentration by ≥ 2 g/dL below the baseline value.
     - **iv.** Acute splenic sequestration **[documentation required]**; OR
       Note: Acute splenic sequestration is defined by an enlarged spleen, left upper quadrant pain, and an acute decrease in hemoglobin concentration of ≥ 2 g/dL below the baseline value.
     - **v.** Acute priapism lasting > 2 hours and requiring a visit to a medical facility **[documentation required]**; AND

H) Patient does **not** have the following (i, ii, iii, and iv):
- **i.** Clinically significant and active bacterial, viral, fungal, or parasitic infection; AND
- **ii.** Advanced liver disease **[documentation required]**; AND
  Note: Examples of advanced liver disease include alanine transaminase > 3 times upper limit of normal; direct bilirubin value > 2.5 times upper limit of normal; baseline prothrombin time (international normalized ratio [INR]) > 1.5 times upper limit of normal; cirrhosis; bridging fibrosis; or active hepatitis.
- **iii.** Severe cerebral vasculopathy as defined by history of untreated Moyamoya disease or presence of Moyamoya disease that puts the patient at risk of bleeding, per the prescribing physician; AND
- **iv.** Prior or current malignancy, myeloproliferative disorder, or significant immunodeficiency disorder; AND

I) According to the prescribing physician, patient will have been discontinued from the following medications (for the duration noted) [i and ii]:
- **i.** Disease-modifying therapies for sickle cell disease for at least 2 months before the planned start of mobilization and conditioning; AND
  Note: Examples of disease-modifying therapies for sickle cell disease include hydroxyurea, Adakveo, L-glutamine, and Oxbryta.
- **ii.** Iron chelation therapy for at least 7 days prior to myeloablative conditioning; AND
  Note: Examples of iron chelators used for this condition include deferoxamine injection, deferiprone tablets or solution, and deferasirox tablets.

J) According to the prescribing physician, patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient will undergo mobilization, apheresis, and myeloablative conditioning; AND
- **ii.** A hematopoietic stem cell mobilizer will be utilized for mobilization; AND
  Note: Mozobil (plerixafor subcutaneous injection) is an example of a hematopoietic stem cell mobilizer.
- **iii.** Busulfan will be used for myeloablative conditioning; AND
- **iv.** Sickle hemoglobin level will be < 30% of total hemoglobin with total hemoglobin concentration ≤ 11 g/dL at BOTH of the following timepoints (a and b):
  - **a)** Prior to planned start of mobilization; AND
  - **b)** Until initiation of myeloablative conditioning; AND

K) Prior to collection of cells for manufacturing, cellular screening is negative for ALL of the following (i, ii, iii, and iv):
- **i.** Human immunodeficiency virus-1 and -2 **[documentation required]**; AND
- **ii.** Hepatitis B virus **[documentation required]**; AND
  Note: A patient who has been vaccinated against hepatitis B virus (HBV) [HBV surface antibody-positive] who is negative for other markers of prior HBV infection (e.g., negative for HBV core antibody) is eligible; a patient with past exposure to HBV is also eligible as long as patient is negative for HBV DNA.
- **iii.** Hepatitis C virus **[documentation required]**; AND
- **iv.** Human T-lymphotrophic virus-1 and -2 **[documentation required]**; AND

L) According to the prescribing physician, patient meets ONE of the following (i or ii):
- **i.** A female† of reproductive potential meets BOTH of the following (a and b):
  - **a)** A negative serum pregnancy test will be confirmed prior to the start of each mobilization cycle and re-confirmed prior to myeloablative conditioning; AND
  - **b)** Patient will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Casgevy; OR
- **ii.** A male† of reproductive potential will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Casgevy; AND

M) The medication is prescribed by a hematologist or a stem cell transplant physician; AND

N) Current patient body weight has been obtained within 30 days **[documentation required]**; AND

O) If criteria A through N are met, approve one dose of Casgevy by intravenous infusion to provide a one-time (per lifetime) single dose, which contains a minimum of 3 x 10^6 CD34+ cells/kg of body weight **[verification required]**.
Note: A single dose of Casgevy is composed of one or more vial(s).

† Refer to the Policy Statement.

2. Transfusion-Dependent Beta-Thalassemia. Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, and P):

A) Patient is ≥ 12 years and < 51 years of age; AND

B) Patient has not received a gene therapy for beta-thalassemia in the past **[verification in claims history required]**; AND
Note: If no claim for Casgevy or Zynteglo (betibeglogene autotemcel intravenous infusion) is present (or if claims is not available), the prescribing physician confirms that the patient has not previously received Casgevy or Zynteglo.

C) According to the prescribing physician, a hematopoietic stem cell transplantation is appropriate for the patient; AND

D) Patient meets ONE of the following (i or ii):
- **i.** Patient does not have a Human Leukocyte Antigen (HLA)-matched donor; OR
- **ii.** Patient has a HLA-matched donor, but the individual is not able or is not willing to donate; AND

E) Patient has ONE of the following genotypes as confirmed by genetic testing (i or ii):
- **i.** Non-β^0/β^0 genotype **[documentation required]**; OR
  Note: Examples include β^0/β^+, β^E/β^0, and β^+/β^+.
- **ii.** β^0/β^0 genotypes **[documentation required]**; AND
  Note: Other examples include $\beta^0/\beta^{+(IVS\text{-}I\text{-}110)}$ and $\beta^{+(IVS\text{-}I\text{-}110)}/\beta^{+(IVS\text{-}I\text{-}110)}$.

F) Patient is transfusion-dependent, as defined by meeting ONE of the following (i or ii):
- **i.** Receipt of transfusions of ≥ 100 mL per kg of body weight of packed red blood cells per year in the previous 2 years **[documentation required]**; OR
- **ii.** Receipt of transfusions of ≥ 10 units of packed red blood cells per year in the previous 2 years **[documentation required]**; AND

G) Patient meets BOTH of the following (i and ii):
- **i.** Patient has been evaluated for the presence of severe iron overload **[documentation required]**; AND
- **ii.** Patient does not have evidence of severe iron overload; AND
  Note: Examples include abnormal myocardial iron results (a T2*-weighted magnetic resonance imaging measurement of myocardial iron of less than 10 msec); high liver iron concentration (≥ 15.5 mg/g); liver biopsy results suggest abnormalities; or clinical evidence of organ damage (e.g., endocrine comorbidities).

H) Patient does not currently have an active bacterial, viral, fungal, or parasitic infection; AND

I) Patient does not have the following (i and ii):
- **i.** Prior or current malignancy, myeloproliferative disorder, or significant immunodeficiency disorder; AND
  Note: This does not include adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin.
- **ii.** Advanced liver disease **[documentation required]**; AND
  Note: Examples include alanine transaminase or aspartate transaminase greater than three times upper limit of normal, direct bilirubin value greater than three times upper limit of normal, active hepatitis, extensive bridging fibrosis, or cirrhosis.

J) According to the prescribing physician, patient will have been discontinued from iron chelation therapy for at least 7 days prior to myeloablative conditioning; AND

Note: Examples of iron chelators used for this condition include deferoxamine injection, deferiprone tablets or solution, and deferasirox tablets.

K) According to the prescribing physician, patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient will undergo mobilization, apheresis, and myeloablative conditioning; AND
- **ii.** A granulocyte-colony stimulating factor product and a hematopoietic stem cell mobilizer will be utilized for mobilization; AND
  Note: Filgrastim products are examples of a granulocyte-colony stimulating factor therapy and Mozobil (plerixafor subcutaneous injection) is an example of a hematopoietic stem cell mobilizer.
- **iii.** Busulfan will be used for myeloablative conditioning; AND
- **iv.** Total hemoglobin level is ≥ 11 g/dL at BOTH of the following timepoints (a and b):
  - **a)** Prior to mobilization; AND
  - **b)** Prior to myeloablative conditioning; AND

L) Prior to collection of cells for manufacturing, cellular screening is negative for ALL of the following (i, ii, iii, and iv):
- **i.** Human immunodeficiency virus-1 and -2 **[documentation required]**; AND
- **ii.** Hepatitis B virus **[documentation required]**; AND
- **iii.** Hepatitis C virus **[documentation required]**; AND
- **iv.** Human T-lymphotropic virus-1 and -2 **[documentation required]**; AND

M) According to the prescribing physician, patient meets ONE of the following (i or ii):
- **i.** A female† of reproductive potential meets BOTH of the following (a and b):
  - **a)** A negative serum pregnancy test will be confirmed prior to the start of each mobilization cycle and re-confirmed prior to myeloablative conditioning; AND
  - **b)** Patient will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Casgevy; OR
- **ii.** A male† of reproductive potential will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Casgevy; AND

N) The medication is prescribed by a hematologist or a stem cell transplant physician; AND

O) Current patient body weight has been obtained within 30 days **[documentation required]**; AND

P) If criteria A through O are met, approve one dose of Casgevy by intravenous infusion to provide a one-time (per lifetime) single dose, which contains a minimum of 3×10^6 CD34+ cells/kg of body weight **[verification required]**.
Note: A single dose of Casgevy is composed of one or more vial(s).

† Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Casgevy is not recommended in the following situations:

1. **Prior Hematopoietic Stem Cell Transplantation.**
   Note: Prescribing physician must confirm that the patient has not received a prior hematopoietic stem cell transplantation.
   Casgevy has not been studied in a patient who has received a prior allogeneic or autologous hematopoietic stem cell transplant. Treatment with Casgevy is not recommended.

2. **Prior Receipt of Gene Therapy.** Casgevy has not been studied in a patient who has received prior gene therapy such as Lyfgenia® (lovotibeglogene autotemcel intravenous infusion) and Zynteglo® (betibeglogene autotemcel intravenous infusion). Treatment with Casgevy is not recommended.

3. **Concurrent Use with Reblozyl® (luspatercept-aamt subcutaneous injection)**. Reblozyl was not utilized with Casgevy in the pivotal trial assessing the efficacy of Casgevy in patients with transfusion-dependent beta-thalassemia.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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