DR.020.B Casgevy® (exagamglogene autotemcel)

Original Implementation Date : 08/21/2024
Version [B] Date : 08/21/2025
Last Reviewed Date: 08/20/2025

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans/Health Partners Plans lines of business unless noted below.

Gene therapy is a benefit exclusion for Individual and Family (ACA) product lines and therefore, non-covered.

POLICY STATEMENT

The Plan considers Casgevy® (exagamglogene autotemcel) medically necessary for its FDA approved indications when the prior authorization listed in this policy are met.

FDA APPROVED INDICATIONS

Gene Therapy is the introduction, removal, or change in the content of a person's genetic code with the goal of treating or curing a disease. It includes therapies such as gene transfer, gene modified cell therapy, and gene editing.

Casgevy® is an autologous genome edited hematopoietic stem cell-based gene therapy indicated for the treatment of patients aged 12 years and older with:

- Sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs)
- Transfusion-dependent

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

Prior authroization is required for Casgevy® (exagamglogene autotemcel). Requests for prior authorization of Casgevy® (exagamglogene autotemcel) will be approved for 18 months for 1 infusion.

Casgevy® (exagamglogene autotemcel) may be considered medically necessary when **ALL** of the following apply:

1. Is prescribed Casgevy® (exagamglogene autotemcel) for an indication that is included in the U.S. Food and Drug Administration (FDA)-approved package labeling; **AND**

2. Is age-appropriate according to FDA-approved package labeling; **AND**

3. Is prescribed a dose and number of treatments that are consistent with FDA-approved package labeling; **AND**

4. Is prescribed Casgevy® (exagamglogene autotemcel) by a specialist at an authorized treatment center for Casgevy® (exagamglogene autotemcel); **AND**

5. Does not have a contraindication to the prescribed medication; **AND**

6. Is not a prior recipient of gene therapy or an allogeneic hematopoietic stem cell transplant; **AND**

7. **One** of the following:

    a. For treatment of sickle cell disease, **both** of the following:

        i. Has sickle cell disease with a βS/βS, βS/β0, or βS/β+ genotype

        ii. **One** of the following:

            a) Has a history of vaso-occlusive episodes (e.g., pain crises, acute chest syndrome, splenic sequestration, priapism) that required a medical facility visit (e.g., emergency department, hospital).

            b) Is currently receiving chronic transfusion therapy for recurrent vaso-occlusive episodes.

    b. For treatment of transfusion-dependent β-thalassemia, **both** of the following:

i. Has genetic testing confirming diagnosis of β-thalassemia.

ii. Has a history of at least 100 mL/kg/year or 8 transfusion episodes/year of packed red blood cell transfusions in the prior 2 years.

DOSAGE AND ADMINISTRATION

Casgevy® is a cell suspension for intravenous infusion. The minimum recommended dose of Casgevy® is 3×10^6 CD34+ cells per kg of body weight, which may be composed of multiple vials.

Administration:

- Administer each vial of Casgevy® via intravenous infusion within 20 minutes of thaw.
- Full myeloablative conditioning must be administered between 48 hours and 7 days before infusion.
- Prophylaxis for seizures should be considered prior to initiating myeloablative conditioning.
- Verify that the patient's identity matches the unique patient identification information on the product labels and lot information sheet prior to thaw and infusion
- Do not sample, alter, or irradiate Casgevy ®
- Do not use an in-line blood filter when infusing Casgevy®

Dose:

- The minimum recommended dose of Casgevy® is 3×10^6 CD34+ cells per kg of body weight, which may be composed of multiple vials.

RISK FACTORS/SIDE EFFECTS

The most common Grade 3 or 4 non-laboratory adverse reactions (incidence ≥ 25%) were mucositis and febrile neutropenia in patients with SCD and TDT, and decreased appetite in patients with SCD.

The most common Grade 3 or 4 laboratory abnormalities (≥ 50%) were neutropenia, thrombocytopenia, leukopenia, anemia, and lymphopenia.

Drug Interactions:

- ***Granulocyte-Colony Stimulating Factor****:* Granulocyte-Colony Stimulating Factor (G-CSF) must not be used for CD34+ HSC mobilization of patients with SCD.

- ***Hydroxyurea****:* Discontinue hydroxyurea at least 8 weeks prior to start of mobilization and conditioning.

- ***Iron Chelators****:* Discontinue iron chelators at least 7 days prior to initiation of myeloablative conditioning. Avoid the use of non-myelosuppressive iron chelators for at least 3 months and use of myelosuppressive iron chelators for at least 6 months after infusion.

- ***Voxelotor and Crizanlizumab:*** Discontinue the use of voxelotor and crizanlizumab at least 8 weeks prior to start of mobilization and conditioning.

MONITORING

1. **Neutrophil Engraftment Failure**: Monitor absolute neutrophil counts (ANC) after infusion. Administer rescue cells in the event of neutrophil engraftment failure.

2. **Delayed Platelet Engraftment:** Monitor platelet counts until platelet engraftment and recovery are achieved. Patients should be monitored for bleeding.

3. **Hypersensitivity Reactions:** Monitor for hypersensitivity reactions during and after infusion.

4. **Off-Target Genome Editing Risk**: Although not observed in healthy donors and patients, the risk of unintended, off-target editing in CD34+ cells due to genetic variants cannot be ruled out.

CLINICAL EVIDENCE

Sickle Cell Disease

In an ongoing single-arm, multi-center trial the safety and efficacy of a single dose of Casgevy™ was evaulated. The study enrolled 63 adult and adolscent patient with sickle cell disease. 58 patients were eligble to undergo mobilization and aphereises to collect their stem cells to manufacture the therapy. 44 patients received the infusion and formed the full analysis set. 31/44 had adequate follow-up to allow evaluation of the primary efficacy endpoint and formed the primary efficacy set. The primary efficacy outcome was the proportion of VF12 responders, defined as patients who did not experience any protocol-defined severe VOCs for at least 12 consecutive months within the first 24 months after CASGEVY infusion. The VF12 response rate was 29/31 (93.5%, 98% one-sided CI: 77.9%, 100.0%). The 29 VF12 responders did not experience protocol-defined severe VOCs during the evaluation period with a median duration of 22.2 months at the time of the interim analysis. Of the 31 patients evaluable for VF12 response, one patient was not evaluable for HF12 response; the remaining 30 patients (100%, 98% one-sided CI: 87.8%, 100.0%) achieved the endpoint of HF12.

Transfusion-dependent β-thalassemia

In an an ongoing open-label, multi-center, single-arm trial the safety and efficacy of of Casgevy®was evaulated. The study entrolled 59 adult and adolescent patients with transfusion-dependent β-thalassemia elligible for mobilization and apheresis to collect CD34+ stem cells for Casgevy® manufacturing. 59 patients started mobilization. A total of 52 (88%) patients received Casgevy® infusion and formed the full analysis set (FAS). 35/52 patients from the FAS (67%) had adequate follow-up to allow evaluation of the primary efficacy endpoint and formed the primary efficacy set. The primarcy outcom was proportion of patients achieving transfusion independence for 12 consecutive months (TI12), defined as maintaining weighted average Hb ≥9 g/dL without RBC transfusions for at least 12 consecutive months any time within the first 24 months after the infusion. The TI12 responder rate was 32/35 (91.4%, 98.3% one-sided CI: 75.7%, 100%). All patients who achieved TI12 remained transfusion-independent, with a median (min, max) duration of transfusion-independence of 20.8 (13.3, 45.1) months and normal mean weighted average total Hb levels (mean [SD] 13.1 [1.4] g/dL).

BACKGROUND

Sickle cell disease is an inherited group of blood disorders caused by a hemglobin defect known as Hemglobin S that replaces both β-globin subunits in hemoglobin. This disease affects roughly 100,000 people in the US and is most commonly in black americans but also hispanic americans at a less prevalent rate. The mutation causes red blood cells to become rigid and have a sickle shape which makes it difficult and painful to pass through small blood vesels as they get stuck and clog blood flow. This blockage can results in many complications as it restricts blood supply to tissues preventing oxygenation. It could cause severe pain and damgage to oragans and joints. This is referred to vaso-occulsive events (VOEs) or vaso-occulsive crises (VOCs), which can be life-threatening if left unresolved. Sickle cell disases requires treatment in clinical settings that specialize in preventing and managing complications from sickle cell diseases. Patients often require blood transfusions, pain management, and preventive measures for infections. Other treatments may be bone marrow transplant, monoclonal antibodies, and gene therapies.

Thalassemia is an inherited blood disorder characterized by decreased hemoglobin production. There are two main types: α-thalassaemia and β-thalassaemia. α-thalassaemia occurs if genes related to α-globin protein are altered or missing and β-thalassaemia is similar as it occurs when the β-globin protein is affected. With these two types there are three major subtypes: thalassemia major, intermedia and minor.

Both the α-globin and β-globin link with eachother to form adult hemoglobin and form a minor fraction of adult hemoglobin which forms fetal hemoglobin. If production of either globins decreases there will be unpaired globin chains which will cause them to accumulate within the developing red cell. If α-globin are not being produced there will be excess β-globin chains (α-thalassaemia) and when β-globin chains are not produced there is an excess of α-globin chains (β-thalassaemia). When these excess chains accumulate in the red cells it results in destruction and reduces the availablility of hemoglobin to carry oxygen, referred to as anemia. To correct this a blood transfusion is usually required. Transfusion-dependent β-thalassemia is the most severe form of β-thalassemia. In this case the anemia must be corrected with regular blood transfusions or else the patient will die early in life.

Casgevy® is the first FDA-approved therapy utilizing CRISPR/Cas9. It is a a cellular gene therapy consisting of autologous CD34+ HSCs edited by CRISPR/Cas9-technology at the erythroid specific enhancer region of the BCL11A gene to reduce BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) protein production. It is prepared from the patient's own HSCs, which are obtained via apheresis procedure(s). The autologous cells are enriched for CD34+ cells, and then genome edited ex vivo by introducing the CRISPR/Cas9 ribonucleoprotein (RNP) complex by electroporation.

In patients with severe sickle cell disease, HbF expression reduces intracellular hemoglobin S (HbS) concentration, preventing the red blood cells from sickling and addressing the underlying cause of disease, thereby eliminating VOCs. In patients with transfusion-dependent β-thalassemia, γ-globin production improves the α-globin to non-α-globin imbalance thereby reducing ineffective erythropoiesis and hemolysis and increasing total hemoglobin levels, addressing the underlying cause of disease, and eliminating the dependence on regular red blood cell (RBC) transfusions.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
N/A	N/A

HCPCS Code	Description
J3392	Injection, exagamglogene autotemcel, per treatment

ICD-10 Codes	Description
D56.1	Beta thalassemia
D57.00	Hb-SS disease with crisis, unspecified
D57.01	Hb-SS disease with acute chest syndrome
D57.02	Hb-SS disease with splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.04	Hb-SS disease with dactylitis
D57.09	Hb-SS disease with crisis with other specified complication

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed by us to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change. For Health Partners Plans Medicaid and Health Partners Plans Chip products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2025 Annual Review. HCPCS and ICD 10 codes added.	B	08/21/2025
New policy.	A	08/21/2024

REFERENCES

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3. Cappellini MD, Farmakis D, Porter J, Taher A, eds. 2021 Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT). 4th ed. Thalassaemia International Federation (TIF). Available at: https://thalassaemia.org.cy/. Accessed March 2024.

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