Casgevy® (exagamglogene autotemcel)
(Intravenous)

Document Number: IC-0744

Last Review Date: 01/06/2026
Date of Origin: 01/04/2024
Dates Reviewed: 01/2024, 02/2024, 01/2025, 02/2025, 07/2025, 01/2026

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for one treatment course (1 dose of Casgevy).
- Renewal: Prior authorization validity may not be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPS Unit]:

- 1 billable unit for one dose

III. Initial Approval Criteria [1]

Submission of supporting clinical documentation (including but not limited to medical records, chart notes, lab results, and confirmatory diagnostics) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission as part of the evaluation of this request. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic, and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax. Failure to submit the medical records may result in the denial of the request due to inability to establish medical necessity in accordance with policy guidelines.

Prior authorization validity is provided in the following conditions:

- Patient is at least 12 years of age; **AND**
- Provider has considered use of prophylaxis therapy for seizures with agents other than phenytoin prior to initiating myeloablative conditioning; **AND**
- Patient has been screened and found negative for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
- Provider will confirm that patient will not receive live vaccines concurrently while immunosuppressed; **AND**
- Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; **AND**

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- Patient has not received other gene therapies used for the treatment of sickle cell disease OR beta thalassemia [e.g., Lyfgenia® (lovotibeglogene autotemcel), Zynteglo® (betibeglogene autotemcel), etc.]**§**; **AND**
- Patient will not receive therapy concomitantly with any of the following:
    - Iron chelators for at least 7-days prior to myeloablative conditioning and for 6 months post-treatment for myelosuppressive iron chelators (e.g., deferiprone) OR 3-months post-treatment for non-myelosuppressive iron chelators; **AND**
    - Disease-modifying agents (e.g., hydroxyurea or crizanlizumab) for at least 8-weeks prior to mobilization and conditioning; **AND**
- Patient is a candidate for autologous hematopoietic stem cell transplant (HSCT) and has not had prior HSCT; **AND**
- Patient does not have a known and available suitable 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic HSCT; **AND**

§ *Requests for subsequent use of exagamglogene after receipt of other gene therapies for sickle cell disease or beta thalassemia (e.g., lovotibeglogene, betibeglogene, etc.) will be evaluated on a case-by-case basis*

Sickle Cell Disease † Φ [1,3]

- Patient has a confirmed diagnosis of sickle-cell disease (includes genotypes βS/βS or βS/β0 or βS/β+) as determined by one of the following:
    - Identification of significant quantities of hemoglobin S (HbS) with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
    - Identification of biallelic *HBB* pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**
- Patient has uncontrolled disease despite treatment with hydroxyurea and crizanlizumab *(Note: trial of crizanlizumab not applicable to patients less than 16 years of age)* OR has required repeat transfusions to treat symptomatic disease and/or reduce the risk of stroke; **AND**
- Patient will be transfused prior to apheresis to a total hemoglobin (Hb) ≤ 11 g/dL and a HbS level < 30% and patient will be transfused at least 8 weeks prior to initiation of myeloablative conditioning (with aforementioned Hb and HbS goals); **AND**
- Patient will not receive granulocyte-colony stimulating factor (G-CSF) for the mobilization of hematopoietic stem cells (HSC); **AND**
- Patient has severe, symptomatic disease despite treatment with supportive care measures, as experienced by one or more of the following:
    - Patient has echocardiographic evidence of a tricuspid regurgitant jet velocity (TRJV) of > 2.5 m/s ; **OR**
    - Patient has had or has a history of an overt stroke (Note: Defined as a sudden neurologic change lasting more than 24 hours that is accompanied by cerebral MRI changes); **OR**

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- Patient has experienced an 'acute chest syndrome' episode, defined as an acute event with pneumonia-like symptoms and the presence of a new pulmonary infiltrate in the previous year, while experiencing treatment failure to hydroxyurea Δ; **OR**
- Patient experienced two or more vaso-occlusive events/crises (VOE/VOC)* in the previous year while experiencing treatment failure to hydroxyurea Δ

**VOE/VOC is defined as an event requiring a visit to a medical facility for evaluation which results in a diagnosis of such being documented due to one (or more) of the following: acute pain, acute chest syndrome, acute splenic sequestration, acute hepatic sequestration, priapism lasting > 2 hours AND necessitating subsequent interventions such as opioid pain management, non-steroidal anti-inflammatory drugs, RBC transfusion, etc.*

Δ Treatment failure to hydroxyurea is defined as experiencing an event despite at least 3 months of therapy OR patient experienced hydroxyurea intolerance defined as the inability to be maintained on an adequate dose due to marrow suppression or severe drug-induced toxicity (e.g., gastrointestinal distress, fatigue, etc.)

Beta Thalassemia † Φ [1,2,11]

- Patient has a documented diagnosis of homozygous beta thalassemia or compound heterozygous beta thalassemia including β-thalassemia/hemoglobin E (HbE) as outlined by the following:
  - Patient diagnosis is confirmed by *HBB* sequence gene analysis showing biallelic pathogenic variants; **OR**
  - Patient has severe microcytic hypochromic anemia, absence of iron deficiency, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A (HbA) and increased HbA_2 with or without increased amounts of hemoglobin F (HbF); **AND**
- Patient has transfusion-dependent disease defined as a history of transfusions of at least 100 mL/kg/year or ≥10 units/year of packed red blood cells (pRBCs) in the 2 years preceding therapy; **AND**
- Patient will be transfused prior to apheresis to a total Hb ≥ 11 g/dL for 60 days prior to myeloablative conditioning; **AND**
- Patient does not have any of the following:
  - Severely elevated iron in the heart (i.e., patients with cardiac T2* less than 10 msec by magnetic resonance imaging [MRI] or left ventricular ejection fraction [LVEF] < 45% by echocardiogram); **OR**
  - Advanced liver disease [i.e., AST or ALT > 3 times the upper limit of normal (ULN), or direct bilirubin value > 2.5 times the ULN, or if a liver biopsy demonstrated bridging fibrosis or cirrhosis]

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

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IV. Renewal Criteria [1]

- Duration of authorization has not been exceeded *(refer to Section I)*.

V. Dosage/Administration [1]

Indication	Dose
Sickle Cell Disease or Beta Thalassemia	Casgevy is provided as a single dose for intravenous infusion containing a suspension of CD34+ cells in one or more vials to achieve the patient-specific dose. Administer all vials. • The minimum recommended dose of Casgevy is 3 × 10^6 CD34+ cells/kg.
- *Sickle Cell Disease: Mobilization should occur using single agent plerixafor* - *Beta Thalassemia: Mobilization should occur using both plerixafor and Granulocyte-Colony Stimulating Factor (G-CSF)* - *Myeloablative conditioning (e.g., busulfan) should not occur until Casgevy (and back-up cell collection) are received. Prophylaxis for hepatic veno-occlusive disease (VOD)/hepatic sinusoidal obstruction syndrome should be considered prior to initiating busulfan conditioning.* - *Casgevy must be administered between 48 hours and 7 days after the last dose of the myeloablative conditioning.* - *Casgevy is for autologous use only. Before infusion, confirm that the patient's identity matches the unique patient identifiers on the Casgevy vial(s). Do not infuse if the information on the patient-specific label does not match the intended patient.*	

VI. Billing Code/Availability Information

HCPCS Code(s):

- J3392 – Injection, exagamglogene autotemcel, per treatment; 1 billable unit = 1 treatment

NDC:

- Casgevy containing a minimum of 3.0 × 10^6 CD34+ cells/kg of body weight, in one or more vials packaged in carton(s): 51167-0290-xx

VII. References

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D56.1	Beta thalassemia
D56.5	Hemoglobin E-beta thalassemia

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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
D57.1	Sickle-cell disease without crisis
D57.20	Sickle-cell/Hb-C disease without crisis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement
D57.214	Sickle-cell/Hb-C disease with dactylitis
D57.218	Sickle-cell/Hb-C disease with crisis with other specified complication
D57.219	Sickle-cell/Hb-C disease with crisis, unspecified
D57.40	Sickle-cell thalassemia without crisis
D57.411	Sickle-cell thalassemia, unspecified, with acute chest syndrome
D57.412	Sickle-cell thalassemia, unspecified, with splenic sequestration
D57.413	Sickle-cell thalassemia, unspecified, with cerebral vascular involvement
D57.414	Sickle-cell thalassemia, unspecified, with dactylitis
D57.418	Sickle-cell thalassemia, unspecified, with crisis with other specified complication
D57.419	Sickle-cell thalassemia, unspecified, with crisis
D57.42	Sickle-cell thalassemia beta zero without crisis
D57.431	Sickle-cell thalassemia beta zero with acute chest syndrome
D57.432	Sickle-cell thalassemia beta zero with splenic sequestration
D57.433	Sickle-cell thalassemia beta zero with cerebral vascular involvement
D57.434	Sickle-cell thalassemia beta zero with dactylitis
D57.438	Sickle-cell thalassemia beta zero with crisis with other specified complication
D57.439	Sickle-cell thalassemia beta zero with crisis, unspecified
D57.44	Sickle-cell thalassemia beta plus without crisis
D57.451	Sickle-cell thalassemia beta plus with acute chest syndrome
D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
D57.453	Sickle-cell thalassemia beta plus with cerebral vascular involvement
D57.454	Sickle-cell thalassemia beta plus with dactylitis
D57.458	Sickle-cell thalassemia beta plus with crisis with other specified complication
D57.459	Sickle-cell thalassemia beta plus with crisis, unspecified
D57.80	Other sickle-cell disorders without crisis

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D57.811	Other sickle-cell disorders with acute chest syndrome
D57.812	Other sickle-cell disorders with splenic sequestration
D57.813	Other sickle-cell disorders with cerebral vascular involvement
D57.814	Other sickle-cell disorders with dactylitis
D57.818	Other sickle-cell disorders with crisis with other specified complication
D57.819	Other sickle-cell disorders with crisis, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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