Medical Policy:

Casgevy (exagamglogene autotemcel) intravenous infusion

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.409	April 1, 2024	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Casgevy is an autologous hematopoietic stem cell (HSC)-based gene therapy indicated for the treatment of sickle cell disease in patients ≥ 12 years of age with recurrent vaso-occlusive crises (VOCs).

Length of Authorization

Casgevy is given as a one-time dose (once per lifetime) by IV infusion

Dosing Limits [Medical Benefit]

Casgevy is given as a **one-time dose (once per lifetime)** by IV infusion. The minimum recommended dose of Casgevy is 3 x 10^6 $CD34^+$ cells/kg of body weight.

Guideline

I. INITIAL CRITERIA

Coverage is provided in the following conditions:

1. Patient is at least 12 years of age; **AND**
2. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative

conditioning; **AND**

3. 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**
4. Must not be administered concurrently with live vaccines while immunosuppressed; **AND**
   A. Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; AND
   B. Patient has not received other gene therapies [e.g., Lyfgenia®(lovotibeglogene autotemcel), Zynteglo® (betibeglogene autotemcel), etc.]**; **AND**
   C. Patient will not receive therapy concomitantly with any of the following:
      i. Iron chelators for 7-days prior to mobilization and 6 months post-treatment (3-months post-treatment for non-myelosuppressive iron chelators); **AND**
      ii. Disease-modifying agents (e.g., hydroxyurea, voxelotor, or crizanlizumab) for at least 8-weeks prior to mobilization and conditioning; **AND**
   D. Patient **is** a candidate for autologous hematopoietic stem cell transplant (HSCT) and has not had prior HSCT; AND
   E. Patient does not have a known 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 (e.g., lovotibeglogene, betibeglogene, etc.) will be evaluated on a case-by-case basis

1. **<u>Sickle Cell Disease</u>**

A. 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: (i **OR** ii)
   i. Identification of significant quantities of HbS with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
   ii. Identification of biallelic HBB pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**

B. Patient has symptomatic disease despite treatment with hydroxyurea and add-on therapy (e.g., crizanlizumab, voxelotor, etc.); **AND**

C. Patient experienced two or more vaso-occlusive event/crises (VOE/VOC)* in the previous year while adhering to the above therapy; **AND**

D. Patient will be transfused prior to apheresis to a total 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**

E. Patient will not receive granulocyte-colony stimulating factor (G-CSF) for the mobilization of hematopoietic stem cells (HSC)

2. **<u>Beta Thalassemia</u>**

A. 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: (i **OR** ii);
   i. Patient diagnosis is confirmed by HBB sequence gene analysis showing biallelic pathogenic variants; **OR**
   ii. 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 HbA2 with or without increased amounts of hemoglobin F (HbF); **AND**

B. 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**

C. Patient will be transfused prior to apheresis to a total Hb ≥ 11 g/dL for 60 days prior to myeloablative conditioning; **AND**

D. Patient does not have any of the following (i **OR** ii);

i. 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**

ii. 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]

Applicable Procedure Codes

Code	Description
J3590	Unclassified biologics

Applicable NDCs

Code	Description
51167-0290-09	Casgevy Intravenous vials in carton

ICD-10 Diagnoses

Code	Description
D56.1	Beta thalassemia
D56.5	Hemoglobin E-beta thalassemia
D57.0	Hb-SS disease with crisis
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
D57.2	Sickle-cell/Hb-C disease
D57.20	Sickle-cell/Hb-C disease without crisis
D57.21	Sickle-cell/Hb-C disease with 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
D57.41	Sickle-cell thalassemia, unspecified, with 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
D57.43	Sickle-cell thalassemia beta zero with 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
D57.45	Sickle-cell thalassemia beta plus with 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
D57.81	Other sickle-cell disorders with crisis
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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	4/1/2024	New Policy

References

1. Casgevy [package insert]. Boston, MA; Vertex, Inc., January 2024. Accessed April 2024.