Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Casgevy (exagamglogene autotemcel) Medical Drug Criteria

Professional / Institutional
Original Effective Date: August 1, 2024
Latest Review Date: November 21, 2024
Current Effective Date: November 21, 2024

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

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.*

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

I. Length of Authorization

Coverage will be provided for one treatment course (1 dose of Casgevy) and will not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- A single dose of Casgevy containing a minimum of 3.0×10^6 CD34+ cells/kg of body weight, in multiple vials

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

- A single dose of Casgevy containing a minimum of 3.0×10^6 CD34+ cells/kg of body weight, in multiple vials

III. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. 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.

Coverage is provided in the following conditions:

- Patient is at least 12 years of age; **AND**
- Provider has considered use of prophylaxis therapy for seizures 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**
- Must not be administered concurrently with live vaccines while immunosuppressed; **AND**
- Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; **AND**
- Patient has not received other gene therapies [e.g., Lyfgenia®(lovotibeglogene autotemcel), Zynteglo® (betibeglogene autotemcel), etc.]**; **AND**
- Patient will not receive therapy concomitantly with any of the following:

  - Iron chelators for 7-days prior to mobilization and 6 months post-treatment (3-months post-treatment for non-myelosuppressive iron chelators); **AND**
  - Disease-modifying agents (e.g., hydroxyurea, voxelotor, 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**
- For patients under 18 years of age, the patient does not have a known and suitable 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic HSCT; **AND**

Sickle Cell Disease † Φ

- Patient has a confirmed diagnosis of sickle-cell disease with one of the following genotypes ßS/ßS or ßS/ß0 or ßS/ß+ (Note: Additional genotypes will be considered on a case-by-case basis based on disease severity) as determined by one of the following:
  - Identification of significant quantities of HbS with or without an additional abnormal ß-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 symptomatic disease despite treatment with hydroxyurea at any point in the past OR add-on therapy (e.g., crizanlizumab, voxelotor, etc.) OR has experienced intolerance; **AND**
- Patient experienced two or more vaso-occlusive event/crises (VOE/VOC)***** in the previous year; **AND**
- 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**
- Patient will not receive granulocyte-colony stimulating factor (G-CSF) for the mobilization of hematopoietic stem cells (HSC)

*****_*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.*_

Beta Thalassemia † [1,10,12]

- Patient has a documented diagnosis of homozygous beta thalassemia or compound heterozygous beta thalassemia including ß-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]

** *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*

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

IV. Renewal Criteria [1,3]

- Coverage cannot be renewed.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CLINICAL RATIONALE

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

REFERENCES

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

HCPCS:

- J3590 – Unclassified biologics
- C9399 – Unclassified drugs or biologicals *(for hospital outpatient use ONLY)*

NDC:

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

REVISIONS	
Posted 07-01/2024 Effective 08-01-2024	New medical policy added to the bcbsks.com web site. Policy maintained by Prime Therapeutics LLC.
Posted 10-22-2024 Effective 11-21-2024	Clinical Criteria Updated. Section I: Length of Authorization ▪ Changed "may not" to "will not" Section III: Initial Approval Criteria ▪ Added criteria requirement that patient has not had a prior HSCT ▪ Added criteria that for patients under the age of 18, the patient must not have a known and suitable 10/10 human leukocyte antigen matched related donor willing to participate in an allogenic HSCT ▪ Added criteria requirement for sickle cell disease that patient must have symptomatic sickle cell disease despite treatment with hydroxyurea or has an intolerance to hydroxyurea ▪ Added criteria requirement that patient will be transfused prior to apheresis and at least 8 weeks prior to initiation of myeloablative conditioning to meet Hb and HbS goals ▪ Removed criteria requirement that patients with 4 events/crises within the past 24 months would meet criteria (now must have 2 or more within the last year)