

Clinical Policy: Exagamglogene Autotemcel (Casgevy)**Reference Number: LA.PHAR.603****Effective Date:****Last Review Date: 02.22.24****Line of Business: Medicaid****[Coding
Implications
Revision Log](#)****See [Important Reminder](#) at the end of this policy for important regulatory and legal information.******Please note: This policy is for medical benefit******Description****Exagamglogene autotemcel (CasgevyTM) is an autologous CD34+ hematopoietic stem and progenitor cell-based therapy.****FDA Approved Indication(s)****Casgevy is indicated for the treatment of sickle cell disease (SCD) in patients 12 years and older with recurrent vaso-occlusive crises (VOCs).****Policy/Criteria****Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.****All requests reviewed under this policy require medical director review.****It is the policy of Louisiana Healthcare Connections[®] that Casgevy is medically necessary when the following criteria are met:****I. Initial Approval Criteria****A. Sickle Cell Disease (must meet all):**

- 1. Diagnosis of SCD with genetic confirmation of one of the following genotypes (a or b):**
 - a. β^S/β^S ;**
 - b. β^S/β^0 ;**
- 2. Prescribed by or in consultation with a hematologist and transplant specialist;**
- 3. Age \geq 12 years;**
- 4. Documentation of \geq 2 severe VOCs per year during the previous two years, with a severe VOC defined as one of the following (a, b, c, d, or e):**
 - a. An acute pain event that requires a visit to a medical facility and administration of pain medications (e.g., opioids or intravenous non-steroidal anti-inflammatory drugs [NSAIDS]) or packed red blood cell (pRBC) transfusions;**
 - b. Acute chest syndrome (ACS);**
 - c. Priapism lasting $>$ 2 hours and requiring a visit to a medical facility;**

CLINICAL POLICY

Exagamglogene Autotemcel

- d. Splenic sequestration;
 - e. Hepatic sequestration;
 - 5. Failure of hydroxyurea at up to the maximally indicated dose for ≥ 6 months, unless contraindicated or clinically significant adverse effects are experienced* (see Appendix D);
**Myelosuppression and hydroxyurea treatment failure: Myelosuppression is dose-dependent and reversible and does not qualify for treatment failure. NHLBI guidelines recommend a 6-month trial on the maximum tolerated dose prior to considering discontinuation due to treatment failure, whether due to lack of adherence or failure to respond to therapy. A lack of increase in mean corpuscular volume (MCV) and/or fetal hemoglobin (HbF) levels is not indication to discontinue therapy.*
 - 6. Attestation from transplant specialist for both the following (a and b):
 - a. Member understands the risk and benefits of alternative therapeutic options such as allogeneic hematopoietic stem cell transplantation (HSCT);
 - b. Member is clinically stable and eligible to undergo myeloablative conditioning and HSCT;
 - 7. Member has not received prior allogeneic HSCT;
 - 8. Member has not received prior gene therapy;
 - 9. Documentation from within the last 6 months that the member is negative for the presence of the following active infections: HIV, hepatitis B virus, and hepatitis C virus;
 - 10. Member does not have advanced liver disease (see Appendix E);
 - 11. Member does not have current malignancy or immunodeficiency disorder;
 - 12. Dose contains a minimum of 3×10^6 CD34⁺ cells/kg.
- Approval duration: 6 months (one-time infusion per lifetime)

B. Other diagnoses/indications (must meet 1 or 2):

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;
- 2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Sickle Cell Disease

- 1. Continued therapy will not be authorized as Casgevy is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2):

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;

CLINICAL POLICY

Exagamglogene Autotemcel

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies –LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACS: acute chest syndrome

ANC: absolute neutrophil count

CBC: complete blood count

FDA: Food and Drug Administration

HbF: fetal hemoglobin

HIV: human immunodeficiency virus

HSCT: hematopoietic stem cell transplantation

MCV: mean corpuscular volume

NHLBI: National Heart, Lung, and Blood Institute

pRBC: packed red blood cells

SCD: sickle cell disease

ULN: upper limit of normal

VOC: vaso-occlusive crisis

WBC: white blood cells

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<u>hydroxyurea[†]</u>	<u>Age ≥ 18 years</u> <u>Initial: 15 mg/kg/dose PO once daily, rounded to the nearest 500-mg increment*</u> <u>Age 9 months to 17 years</u> <u>Initial: 20 mg/kg/dose PO once daily*</u> <u>* Increase by 5 mg/kg/day every 8 weeks until mild myelosuppression (ANC 2,000 to 4,000/microliter) achieved.</u>	<u>35 mg/kg/day</u>
<u>Droxia® (hydroxyurea)</u>	<u>Age ≥ 18 years</u> <u>Initial: 15 mg/kg/day PO single dose; based on blood counts, may increase by 5 mg/kg/day every 12 weeks to a max 35 mg/kg/day</u>	
<u>Siklos® (hydroxyurea)</u>	<u>Age ≥ 18 years</u> <u>Initial: 15 mg/kg PO QD*</u> <u>Age 2 years to 17 years</u>	

CLINICAL POLICY

Exagamglogene Autotemcel

<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
	<u>Initial: 20 mg/kg PO QD*</u> <u>*Based on blood counts, may increase by 5 mg/kg/day every 8 weeks or if a painful crisis occurs</u>	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

‡ Off-label, 2014 NHLBI SCD guideline-supported dosing regimen

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- **Hydroxyurea dose titration: Members should obtain complete blood counts (CBC) with white blood cell (WBC) differential and reticulocyte counts at least every 4 weeks for titration. The following lab values indicate that it is safe to increase dose.**
 - **Absolute neutrophil count (ANC) in adults $\geq 2,000/\mu\text{L}$, or ANC $\geq 1,250/\mu\text{L}$ in younger patients with lower baseline counts**
 - **Platelet count $\geq 80,000/\mu\text{L}$**

If neutropenia or thrombocytopenia occurs: hydroxyurea dosing is held, CBC and WBC differential are monitored weekly, and members can restart hydroxyurea when values have recovered.

Appendix E: Advanced Liver Disease

- **Examples of advanced liver disease include, but are not limited to, the following:**
 - **Cirrhosis**
 - **Bridging or significant fibrosis**
 - **Active hepatitis**
 - **Persistent aspartate transaminase, alanine transaminase, or direct bilirubin value $> 3\times$ the upper limit of normal (ULN)**
 - **Baseline prothrombin time or partial thromboplastin time $> 1.5\times$ ULN**

V. Dosage and Administration

<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>SCD</u>	<u>Minimum recommended dose: 3×10^6 CD34[±] cells/kg of body weight IV</u>	<u>Not applicable</u>

VI. Product Availability

Single-dose cell suspension: up to nine vials, with each vial containing 4 to 13×10^6 CD34⁺ cells/mL suspended in 1.5 to 20 mL cryopreservative medium

VII. References

CLINICAL POLICY

Exagamglogene Autotemcel

1. Casgevy Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; December 2023. Available at: www.casgevy.com. Accessed December 14, 2023.
2. Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-CaS9 gene editing for sickle cell disease and β -thalassemia. N Engl J Med 2021; 384:252-60. www.doi.org/10.1056/NEJMoa2031054.
3. ClinicalTrials.gov. A safety and efficacy study evaluating CTX001 in subjects with severe sickle cell disease. Last updated June 1, 2022. Available at: <https://clinicaltrials.gov/ct2/show/NCT03745287>. Accessed November 1, 2023.
4. Yawn BP, Buchanan GR, Afeniyi-Annan AN, et al. Evidence-based management of sickle cell disease: Expert Panel Report, 2014. National Heart, Lung, and Blood Institute (NHLBI). Available at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed December 8, 2023.
5. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier. Updated periodically. Available at: <http://www.clinicalkey.com/pharmacology>. Accessed January 8, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<u>HCPCS Codes</u>	<u>Description</u>
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

<u>Reviews, Revisions, and Approvals</u>	<u>Date</u>	<u>LDH Approval Date</u>
Converted corporate to local policy.	02.22.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

CLINICAL POLICY

Exagamglogene Autotemcel

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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