Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 318.0

Section: Medical Benefit Pharmaceutical Policy

Subject: Casgevy (exagamglogene autotemcel)

I. Policy:
Casgevy (exagamglogene autotemcel)

II. Purpose/Objective:
To provide a policy of coverage regarding Casgevy (exagamglogene autotemcel)

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
Casgevy (exagamglogene autotemcel) is a cellular gene therapy consisting of autologous CD34+ hematopoietic cells edited by CRISPR/Cas9 technology to create a DNA double-strand break at a critical transcription binding site of the erythroid-specific enhancer region of the BCL11A gene. This modification reduces BCL11A expression in the erythroid lineage, allowing for increased γ-globin expression and fetal hemoglobin (HbF) production in erythroid cells. After exagamglogene autotemcel infusion, the edited CD34+ cells engraft in the bone marrow and differentiate to erythroid lineage cells with reduced BCL11A expression. In patients with severe sickle cell disease, HbF expression reduces intracellular hemoglobin S concentration, preventing the RBCs from sickling and addressing the underlying cause of disease, thereby eliminating veno-occlusive crises. In transfusion-dependent beta-thalassemia, γ-globin production improves the imbalance in α-globin to non-α-globin, leading to improved erythropoiesis and increasing total Hb levels.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

Casgevy (exagamglogene autotemcel) will be considered medically necessary for the Commercial, Exchange, and CHIP lines of business when ALL of the following criteria are met:

Sickle Cell Disease
- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years **AND**
    - Documentation of therapeutic failure, contraindication, or intolerance to hydroxyurea

  AND
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Lyfgenia) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

Transfusion-Dependent β-thalassemia
- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of transfusion-dependent β-thalassemia AND medical record documentation of a history of ≥ 100 mL/kg/year or 10 units/year of packed red blood cell (RBC) transfusions in the prior 2 years **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Zynteglo) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

*Note to reviewer: The package insert recommends confirming that hematopoietic stem cell transplantation (HSCT) is appropriate prior to Casgevy since patients will be going through similar steps (mobilization, apheresis, and myeloablative) required for a HSCT. However, the clinical trials excluded patients who had a known and available HLA-matched related donor. Considering that HSCT has been available for longer and has more evidence supporting its use, it may be appropriate to require HSCT as an alternate to Casgevy. While it is possible for patients to have a matched unrelated donor, outcomes are best with matched related donors.

**Note to reviewer: In clinical trials, VOCs were defined as:
- Acute pain event requiring a visit to a medical facility and administration of pain medications (opioids or intravenous [IV] non-steroidal anti-inflammatory drugs [NSAIDs]) or RBC transfusions OR
- Acute chest syndrome OR
- Priapism lasting > 2 hours and requiring a visit to a medical facility OR
- Splenic sequestration.

AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Casgevy (exagamglogene autotemcel) will be considered medically necessary for the Medicare line of business when ALL of the following criteria are met:

Sickle Cell Disease

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years

  AND
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Lyfgenia) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

Transfusion-Dependent β-thalassemia

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of transfusion-dependent β-thalassemia AND medical record documentation of a history of ≥ 100 mL/kg/year or 10 units/year of packed red blood cell (RBC) transfusions in the prior 2 years **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Zynteglo) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

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AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

REFERENCES:

1. Casgevy [Prescribing Information]. Boston MA. Vertex Pharmaceuticals Incorporated. January 2024.
2. IPD Analytics. Casgevy for the Treatment of Sickle Cell Disease. New Drug Approval Review. January 11, 2024. Accessed January 29, 2024. https://www.ipdanalytics.com
3. A Safety and Efficacy Study evaluating CTXOO1 in Subjects with Severe Sickle Cell Disease [Internet]. Bethesda, MD: US National Library of Medicine. c2023. Available at https://clinicaltrials.gov/study/NCT03745287?term=CTX001&rank=6
4. A Safety and Efficacy Study Evaluating CTX001 in Subjects With Transfusion-Dependent β-Thalassemia [Internet]. Bethesda, MD: US National Library of Medicine. c2023. Available at https://clinicaltrials.gov/study/NCT03655678?term=NCT03655678&rank=1
5. Holmberg L, Deeg, HJ, Sandmaier, B. Determining Eligibility for autologous hematopoietic cell transplantation. UpToDate [database online]. Last updated Mar 07, 2022. Available at http://www.uptodate.com/home/index.html. Accessed May 9, 2024.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 5/21/24

Revised:

Reviewed:

MA UM Committee approval: 8/30/24