CASGEVY (REQUIRES PREAUTHORIZATION)

X.225

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DESCRIPTION

Target Agents:

Casgevy® (exagamglogene autotemcel) is FDA approved for the treatment of patients aged 12 years and older with:

- sickle cell disease (SCD) with recurrent vaso-occlusive crises
- transfusion-dependent β-thalassemia (TDT)

Dates

Original Effective
03-01-2024
Last Review
11-06-2024
Next Review
11-06-2025

POLICY

Initial Evaluation

I. Target Agent(s) may be considered **medically necessary** when **ALL** of the following are met:

A. The patient is at least 12 years old **AND**

B. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning **AND**

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D. Must not be administered concurrently with live vaccines while immunosuppressed **AND**

E. Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40 **AND**

F. 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**

G. The patient will not receive therapy concomitantly with any of the following:

1. Hydroxyurea for at least 2 months prior to mobilization and until all cycles of apheresis are completed (Note: If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning) **AND**

2. Myelosuppressive iron chelators (e.g., deferiprone, etc.) for 7-days prior to mobilization, conditioning, and 6 months post-treatment; 3-months post treatment for non-myelosuppressive iron chelators **AND**

3. Disease-modifying agents (e.g., L-glutamine, vexelotor, crizanlizumab) for at least 2 months prior to mobilization **AND**

4. Prophylactic HIV anti-retroviral therapy (Note: Patients receiving prophylactic ART should stop therapy for at least one month prior to mobilization and until all cycles of apheresis are completed **AND**

5. Mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF);

H. Patient has not received other gene therapy [e.g., Lyfgenia™ (lovotibeglogene autotemcel)] **AND**

I. Patient is a candidate for autologous hematopoietic stem cell transplant (HSCT); **AND**

1. Identification of significant quantities of HbS with or without an additional abnormal β - globin chain variant by hemoglobin assay; **OR**

2. Identification of biallelic HBB pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing;

K. Patient experienced at least 2 vaso-occlusive events/crises (VOE/VOC)* in the previous 12 months while adhering to the above therapy (Note: Patients experiencing four events/crises in the previous 24 months will also have met this requirement

*VOE/VOC is 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.

Length of Approval: 1 per lifetime

CLINICAL RATIONALE

CASGEVY (exagamglogene autotemcel) is a cellular gene therapy consisting of autologous CD34+ HSCs edited by CRISPR/Cas9-technology at the erythroid specific enhancer region of the BCL11A gene to reduce BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) protein production.

CASGEVY is prepared from the patient's own HSCs, which are obtained via apheresis procedure(s). The autologous cells are enriched for CD34+ cells, and then genome edited ex vivo by introducing the CRISPR/Cas9 ribonucleoprotein (RNP) complex by electroporation. The guide RNA included in the RNP complex enables CRISPR/Cas9 to make a precise DNA double-strand break at a critical transcription factor binding site (GATA1) in the erythroid specific enhancer region of the BCL11A gene. As a result of the editing, GATA1 binding is disrupted and BCL11A expression

Sickle Cell Disease Trial 1 (NCT03745287) is an ongoing single-arm, multi-center trial evaluating the safety and efficacy of a single dose of CASGEVY in adult and adolescent patients with sickle cell disease. Eligible patients underwent mobilization and apheresis to collect CD34+ stem cells for CASGEVY manufacture, followed by myeloablative conditioning and infusion of CASGEVY. Patients were then followed in Trial 1 for 24 months after CASGEVY infusion. Patients who complete or discontinue from Trial 1 are encouraged to enroll in Trial 2 (NCT04208529), an ongoing long-term follow-up trial for additional follow up for a total of 15 years after CASGEVY infusion.

At the time of the interim analysis, a total of 63 patients enrolled in the trial, of which 58 (92%) patients started mobilization. A total of 44 (76%) patients received CASGEVY infusion and formed the full analysis set (FAS). Thirty-one patients from the FAS (70%) had adequate follow-up to allow evaluation of the primary efficacy endpoint and formed the primary efficacy set (PES).

The primary efficacy outcome was the proportion of VF12 responders, defined as patients who did not experience any protocol-defined severe VOCs for at least 12 consecutive months within the first 24 months after CASGEVY infusion in Trial 1. The proportion of patients who did not require hospitalization due to severe VOCs for at least 12 consecutive months within the 24-month evaluation period (HF12) was also assessed. The evaluation of VF12 and HF12 began 60 days after the last RBC transfusion for post-transplant support or SCD management. The median (min, max) time to the last RBC transfusion was 19 (11, 52) days following CASGEVY infusion for patients in the primary efficacy set.

The interim analysis occurred at the time when the alpha spending was approximately 0.02 for a one-sided test, when 31 patients were evaluable for VF12 responder status. The VF12 response rate was 29/31 (93.5%, 98% one-sided CI: 77.9%, 100.0%). The 29 VF12 responders did not experience protocol defined severe VOCs during the evaluation period with a median duration of 22.2 months at the time of the interim analysis. One VF12 responder, after initially achieving a VF12 response, experienced an acute pain episode meeting the definition of a severe VOC at Month 22.8 requiring a 5-day hospitalization; this patient was reported to have a parvovirus B19 infection at the time. Of the 31 patients evaluable for VF12 response, one patient was not evaluable for HF12 response; the remaining 30 patients (100% [98% one-sided CI: 87.8%, 100.0%]) achieved the endpoint of HF12.

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REVISIONS

01-02-2025

Added new code for 01/01/2025: J3392