

Molina Clinical Policy

Casgevy (exagamglogene autotemcel) for Sickle Cell Disease:

Policy No. 447

Last Approval: 2/14/2024

Next Review Due By: December 2024



DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. 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 (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Sickle cell disease (SCD) is an inherited (autosomal recessive) hemoglobinopathy characterized by chronic hemolytic anemia and intermittent, painful, vaso-occlusive crisis, (VOC's). A VOC is defined as pain resulting from tissue ischemia caused by vaso-occlusion most commonly in the bone(s) and bone marrow. Those with greater than 3 hospitalizations for VOC per year are at increased risk for early death. Almost all people with sickle cell disease experience one or more vaso-occlusive crises in their lives.

The disease can occur in individuals of any ethnicity, but is most common in those of African, Caribbean, Mediterranean, Middle Eastern, and Indian ancestry. Approximately 1 in 500 African American infants born in the United States are diagnosed with SCD which has led to screening panels in newborns. There are about 100,000 individuals with SCD in the United States. About 20,000 are considered to have severe sickle cell disease. Specific pathogenic mutations in the beta globin gene cause sickle cell anemia. Sixty to seventy percent of SCD diagnosed in the United States are caused by the same homozygous pathogenic variant known as hemoglobin S (HbS).

The trademark laboratory feature of SCD is the presence of sickle-shaped red blood cells on peripheral blood smear. Red blood cells sickle at low oxygen tension which obstructs vessels, incites inflammation, and causes endothelial dysfunction. SCD is the leading cause of ischemic stroke in children. Chronic complications from sickle cell anemia shorten life span by 20 years, on average. Individuals with sickle cell disease also endure stigma and bias in attempting to get care and face additional mental health challenges as they cope with this disorder. (JAMA, 2020, Kavanaugh; Evidence-Based management of sickle cell disease: Expert Panel report, 2014).

Current therapies for sickle cell anemia include Hydroxyurea, L-glutamine (Endari), crizanlizumab (Adakveo), voxelotor (oxbryta) and allogeneic Hematopoietic Stem-cell transplantation (HSCT). Apart from HSCT, all therapies are only partially effective, and none prevent VOCs. In allogeneic HSCT, donors need to be well matched at three or more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1), (Chao, 2022; Deeg & Sandmaier, 2022; Field & Vichinsky, 2022; Negrin, 2022; Rodgers et al., 2022; Khan & Rodgers, 2021; Hayes, 2020). Those without a well-matched donor would not be able to access allogeneic stem cell transplant therapy. Less than 20% of eligible patients have a well-matched donor. HSCT is the only proven curative therapy to date. Gene-cell therapy, which involves the autologous transplantation of genetically modified hematopoietic stem cells, is a new a novel therapeutic option that is potentially curative.

Exagamglogene autotemcel (Casgevy, CTX001) is a new, first in class gene-cell therapy for the treatment of severe sickle cell disease with recurrent VOCs. Casgevy gene-cell therapy modifies a patient's own CD34+ stem cells with the CRISPR/cas9 system to turn on fetal hemoglobin production. Enhanced expression of fetal hemoglobin increases the proportion of functional hemoglobin capable of oxygen transport without the propensity of sickling.

This therapy is not only unique in that it is the first therapy to use CRISPR technology, but also in its target. Casgevy does not directly target or edit the beta globin gene mutation that causes sickle cell anemia. Instead, Casgevy indirectly promotes the expression of fetal hemoglobin (HbF). Fetal hemoglobin is normally expressed until three

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months of age when a repressor appears in development that turns off fetal hemoglobin. After fetal hemoglobin is turned off, adult hemoglobin is produced.

In someone with sickle cell anemia, it is at this transition from fetal to adult hemoglobin that sickling of RBCs can occur and signs and symptoms of sickling develop. Because fetal hemoglobin uses gamma globin instead of beta globin as a carrier of oxygen, the effects of the beta globin mutation are lessened.

If a significant amount of fetal hemoglobin is expressed in adults again, it could partially restore oxygen transport without the tendency of sickle hemoglobin to polymerize, sickle and obstruct vessels.

Casgevy (exa-cel) promotes the expression of gamma globin by removing its natural repressor. Once gamma globin expression is restored, fetal hemoglobin (HbF) is made. Real world evidence supports the clinical benefit of HbF once it reaches 20% or higher of total hemoglobin.

In a nutshell, Casgevy turns back the clock on the developmental switch from fetal hemoglobin to adult hemoglobin by repressing, a repressor of fetal hgb.

The technical genetic details of the mechanism of Casgevy are as follows: Casgevy down regulates or “knocks down” the repressor of gamma globin, called BCL11A. Specifically, Casgevy edits / disrupts an enhancer (noncoding regulatory region) of the BCL11-A gene. By disrupting the enhancer of BCL11-A, BCL11-A expression is reduced and subsequently repression of gamma globin is reduced allowing fetal hemoglobin production. Note, the faulty beta globin gene and its expression are untouched and still produce some degree of hemoglobin with potential to sickle albeit at lower levels. [Casgevy CRISPR/Cas9 therapy is delivered to CD34+ stem cells via electroporation; viral vectors are not used.](#)

FDA approval of Casgevy was based on data from the phase 1/2/3 trial, CLIMB SCD-121. This trial is an international, multicenter, open-label, single arm study (NCT03745287) of 44 patients, ages 12-35 years of age with severe SCD as indicated by both genotype and phenotype. $\beta S/\beta S$, $\beta S/\beta 0$, or $\beta S/\beta +$ are considered severe genotypes. Phenotypically, severe SCD is defined as having a clinical history of ≥ 2 VOCs per year over the previous 2 years.

Forty-four patients received Casgevy, but only 30 had been in the trial long enough to be eligible for the primary efficacy interim analysis. The primary efficacy endpoint was the proportion of subjects without VOCs for a period of 12 months post infusion. All but one of 30 patients had been free of VOCs for 1 year. Fetal and total hemoglobin increased, with a mean of 11.1 g/dL and the proportion of HbF was maintained at $> 40\%$ of total hemoglobin from 6 months on ward. Final data for study 121 will be obtained in the second half of 2025.

Side effects of Casgevy were similar to those that occur with autologous stem cell transplants. There were no significant safety events attributable to Casgevy. Off-target genome editing is a risk and cannot be ruled out.

Administration of Casgevy involves harvesting the patients stem cells, and once outside the body, purifying and editing the patient’s cells. Once enough edited cells are grown, the cells are shipped back to the treatment center in preparation for transfusion into the patient. The patient will then go through standard myeloablation procedures and remain in the hospital after receiving their edited cells while engraftment occurs.

RELATED POLICIES

MCP-448: Lyfgenia (lovotibeglogene autotemcel) for Sickle Cell Disease

MCP-449: Casgevy (exagamglogene autotemcel) for Transfusion Dependent Thalassemia

COVERAGE POLICY

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Casgevy (exa-cel or exagamglogene autotemcel) for the treatment of SCD may be considered medically necessary when ALL of the following clinical criteria with documentation are met:

1. A diagnosis of severe sickle cell disease defined by:
 - a. Genetic testing confirming severe sickle cell disease genotype ($\beta S/\beta S$, $\beta S/\beta 0$, or $\beta S/\beta +$); **AND**
 - b. History of at least two severe vaso-occlusive events per year for the previous two years defined by 2 of the following events while receiving appropriate supportive care (i.e., Hydroxyurea, transfusions):
 - Acute pain event requiring a visit to a medical facility & administration of pain medications (opioids or IV nonsteroidal anti-inflammatory drugs or RBC transfusions); OR
 - Acute chest syndrome indicated by a new pulmonary infiltrate associated with pneumonia -like symptoms, pain, or fever; OR
 - Priapism lasting > 2 hours & requiring a visit to a medical facility; OR
 - Splenic sequestration, defined by an enlarged spleen, left upper quadrant pain and an acute decrease in hemoglobin concentration $\geq 2\text{g/dL}$;

AND
2. Clinical documentation and recent relevant evaluation, labs, and workup establishing eligibility for autologous stem cell transplant including the Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1 (ambulatory and able to carry out work of a light or sedentary nature); OR Karnofsky or Lansky performance status (KPS) of at least 80%; **AND**
 - a. Does not have an HLA matched related donor available; **AND**
 - b. Has not had previous HSCT; **AND**
 - c. Does not have significant active infections or cytopenias (white blood cell count $< 3 \times 10^9/\text{L}$ or platelet count $< 50 \times 10^9/\text{L}$; **AND**
 - d. Does not have a baseline HbF concentration $> 15\%$

AND
3. Adequate and stable renal, liver, lung, and cardiac function as evidenced by recent evaluation and laboratory workup:
 - a. Estimated glomerular filtration rate $\geq 60\text{ml/min}/1.73 \text{ m}^2$; **AND**
 - b. Liver function tests $< 3 \times \text{ULN}$; **AND**
 - c. Direct bilirubin $< 2.5 \times$ the Upper Limit of Normal (ULN); **AND**
 - d. Prothrombin time (INR – International normalized ratio) $\leq 1.5 \times \text{ULN}$; **AND**
 - e. Carbon monoxide diffusion capacity of the lung (DLCO) $\geq 50\%$ (corrected for Hb and or alveolar volume); **AND**
 - f. Left ventricular ejection fraction $\geq 45\%$

AND
4. Member has not received a gene therapy, or is not being considered for other gene therapies, or investigational cellular therapy for sickle cell disease; **AND**
5. Member is 12 years of age or greater, but less than or equal to 35 years of age; **AND**
6. Females of childbearing potential and males capable of fathering a child: Member has been counseled on the use of effective contraception during treatment (from start of mobilization through at least 6 months after administration of Casgevy) AND advised of the risks associated with conditioning agents; **AND**
7. For females of childbearing potential: Member is not pregnant or breast-feeding: Negative serum pregnancy test within the past 30 days

NOTE: A negative serum pregnancy test must be confirmed prior to the start of mobilization and re-confirmed prior to conditioning procedures and before Casgevy administration.

AND

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8. Negative testing for Human Immunodeficiency virus-1 negative, Human Immunodeficiency virus-2 negative, hepatitis B, hepatitis C, syphilis, Human T-Cell lymphotropic virus-1 and Human T-Cell lymphotropic virus-2, malaria, tuberculosis, toxoplasmosis, Trypanosoma cruzi or West Nile Virus.

AND

9. No prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**

10. No History of significant bleeding disorder; **AND**

11. For those patients aged 12-16 years of age, a screening Transcranial Doppler Velocity study in the middle cerebral artery and the internal carotid artery does not indicate a high risk for stroke (TAMMV < 170 cm/sec for non-imaging TCD and <155 cm/sec for imaging TCD); **AND**

12. No History of abnormal TCD in those aged 12-18 years of age (TAMMV \geq 200cm/sec for non-imaging TCD and \geq 185 cm/sec for imaging TCD); **AND**

13. No History of untreated Moyamoya disease or presence of Moyamoya disease at screening that could put the patient at risk for bleeding.

CONTINUATION OF THERAPY

Repeat administration is experimental and investigational since the safety and efficacy beyond one treatment has not been studied and is not indicated in the current FDA approval for Casgevy. The evidence is insufficient to determine the effects on net health outcomes.

LIMITATIONS AND EXCLUSIONS

There are no contraindications listed in the manufacturer's labeling at this time.

The following are considered **experimental, investigational, and unproven** based on insufficient evidence:

1. Any indications other than those listed above (e.g., sickle cell disease)
2. Prior treatment with any form of HSCT, Casgevy, or other gene therapy

DURATION OF APPROVAL: Duration sufficient for **ONE** single course of treatment

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, a board-certified hematologist

AGE RESTRICTIONS: \geq 12 years and \leq 35 years at the time of infusion

The age across the trials was 12 to 35 years of age.

DOSING CONSIDERATIONS: Cell suspension for IV infusion. For autologous use only.

- Patients are required to undergo HSC mobilization followed by apheresis to obtain CD34+ cells for Casgevy manufacturing.
- Dosing is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight. Minimum recommended dose: 3×10^6 CD34+ cells/kg as a one-time IV infusion
- Myeloablative conditioning must be administered before infusion of Casgevy.

ADMINISTRATION:

1. Casgevy is considered a provider-administered therapy in a Qualified Treatment Center by a physician(s) with experience in HSCT and in the treatment of patients with SCD.
2. Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or rendering a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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SUMMARY OF MEDICAL EVIDENCE

Accelerated approval for Casgevy is based on results from interim analysis of one Phase 1/2/3 clinical trial.

Phase 1/2/3 Study Climb-121

The CLIMB SCD-121 trial (NCT03745287) is an international, multicenter, open-label, single arm study of 44 patients, ages 12-35 years of age with severe SCD indicated by both genotype and phenotype. $\beta S/\beta S$, $\beta S/\beta 0$, or $\beta S/\beta +$ are considered severe genotypes. Phenotypically, severe SCD is defined as having a clinical history of ≥ 2 VOCs per year over the previous 2 years. 30 of the 44 patients had been followed long enough at the June 14, 2023, data cut to be included in the analysis.

The primary efficacy endpoint was the proportion of subjects without VOCs for a period of 12 months post infusion. A key secondary endpoint was HF12 (proportion of patients free from inpatient hospitalization for severe VOC for at least 12 months).

29 of 30 (96.7%) patients in the primary efficacy set were free of VOCs for 12 months as of June 14, 2023.

30 of 30 (100%) patients in the primary efficacy set achieved HF12 (Hospitalization free for 12 months).

40 of 40 patients (100%) achieved the surrogate efficacy biomarker goal of HbF $\geq 20\%$ by month 6.

Markers of hemolysis improved with mean LDH normalizing by 9 months.

One patient death was attributed to covid infection potentially complicated by busulfan conditioning. That individual was 33 years old with pre-existing lung disease.

Final data for study 121 will be obtained in the second half of 2025.

Side effects from Casgevy were similar to those that occur with autologous stem cell transplants. This included nausea, stomatitis, vomiting and febrile neutropenia. There were no significant safety events attributable to Casgevy. All patients were successful in neutrophil and platelet engraftment.

Additional molecular safety analyses of Casgevy relied on both in-silico and cell-based assays to assess the potential off-target editing sites throughout the genome. Roughly 5000 potential off target sites were identified by in-silico methods when allowing for imperfect crisper targeting along the genome sequence. Of these, no significant off target cutting or editing could be identified in the cell-based assay. The FDA has noted that the size and quality of the cell samples used in the confirmation analyses was very small ($n= 3$) and may not have fully represented opportunities for off target editing to be seen.

The 15 year long term extension study, CLIMB -131, is an on-going, global, multi-site, rollover study designed to evaluate the safety and efficacy of Casgevy in subjects who previously received Casgevy in study 121 or study 111 (for treatment of transfusion dependent thalassemia). Study 151 has started and is aimed at pediatric patients aged 2-11 years of age with SCD.

National and Specialty Organizations

Institute for Clinical and Economic Review (ICER) published a final evidence report supporting the value of Casgevy for the treatment of sickle cell disease (July 2023). The report focused on the clinical benefits of Casgevy but noted cost-effectiveness comparisons to standard clinical management for severe sickle cell disease, could not be completed without the actual prices of therapies. The systematic review suggests Casgevy is likely to “substantially” improve quality and length of life for patients with severe SCD. The magnitude of this superiority is still uncertain due to known risks with myeloablative conditioning and unknown durability.

National Heart, Lung and Blood Institute management guidelines notes, “The clinical benefit of HSCT or gene therapy vs regular blood transfusion therapy for secondary prevention of cerebral infarcts in children and adults with preexisting silent cerebral infarct should be determined.”

CODING & BILLING INFORMATION

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CPT (Current Procedural Terminology) Codes

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System) Code

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Casgevy (exagamglogene autotemcel (exa-cel))]

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

02/14/2024 Name modified to include "for Sickle Cell Disease."
12/21/2023 New policy. IRO review completed December 2023.

REFERENCES

- Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β -Thalassemia. *N Engl J Med*. 2021 Jan 21;384(3):252-260. doi: 10.1056/NEJMoa2031054. Epub 2020 Dec 5. PMID: 33283989.
- Kavanagh PL, Fasipe TA, Wun T. Sickle Cell Disease: A Review. *JAMA*. 2022 Jul 5;328(1):57-68. doi: 10.1001/jama.2022.10233. PMID: 35788790.
- Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA*. 2014 Sep 10;312(10):1033-48. doi: 10.1001/jama.2014.10517. Erratum in: *JAMA*. 2014 Nov 12;312(18):1932. Erratum in: *JAMA*. 2015 Feb 17;313(7):729. PMID: 25203083.
- Field JJ, Vichinsky EP. Overview of the management and prognosis of sickle cell disease. Updated Sept 26, 2022. <http://www.uptodate.com/>. Accessed September 16, 2023.
- Hayes. Health technology assessment: Exagamglogene Autotemcel (Vertex/CRISPR) for Sickle Cell Disease. Published December 10, 2023. Updated December 11, 2023. <https://evidence.hayesinc.com/report/pg.exacelSCD>. Accessed December 11, 2023.
- Sickle Cell Disease Association of America (SCDAA). What is sickle cell disease (SCD)? <https://www.sicklecelldisease.org/sickle-cell-health-and-disease/types/>. Accessed September 16, 2023.
- Rodgers GP, George A, Strouse J. Hydroxyurea use in sickle cell disease. May 10, 2023. <http://www.uptodate.com>. Accessed September 16, 2023.
- Eastern Cooperative Oncology Group (ECOG) Performance Status. <https://ecog-acrin.org/resources/ecog-performance-status>. Accessed September 16, 2023.
- National Heart, Lung and Blood Institute (NHLBI). Evidence-based management of sickle cell disease: Expert panel report, 2014. <https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease>. Accessed September 16, 2023.
- Cellular, Tissue, and Gene Therapies Advisory Committee Meeting. FDA Briefing Document. BLA 125787 exagamglogene autotemcel. October 31, 2023. <https://www.fda.gov/advisory-committees/advisory-committee-calendar/cellular-tissue-and-gene-therapies-advisory-committee-october-31-2023-meeting-announcement-10312023#event-materials>. Accessed November 2023.
- ClinicalTrials.gov
 - CTX001-121 (NCT03745287). A Safety and Efficacy Study Evaluating CTX001 in Subjects With Severe Sickle Cell Disease. Last updated 12/6/2022. <https://clinicaltrials.gov/study/NCT03745287?rank=5#participation-criteria>. Accessed December 5, 2023
 - CTX001-131 (NCT04208529). <https://classic.clinicaltrials.gov/ct2/show/NCT04208529?term=exagamglogene&draw=2&rank=>. Accessed December 5, 2023
 - CTX001-151 (NCT05329649) <https://classic.clinicaltrials.gov/ct2/show/NCT05329649?term=exagamglogene&draw=2&rank=4>. Accessed December 5, 2023
- DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. *Blood Adv*. 2020 Apr 28;4(8):1554-1588. doi: 10.1182/bloodadvances.2019001142. PMID: 32298430; PMCID: PMC7189278.
- CASGEVY (exagamglogene autotemcel), FDA Prescribing Information December 2023.: <https://www.fda.gov/media/174615/download>

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14. Brandow AM, Carroll CP, Creary S et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. Blood Adv. 2020 Jun 23;4(12):2656-2701. doi: 10.1182/bloodadvances.2020001851. PMID: 32559294; PMCID: PMC7322963.
15. Liem RI, Lanzkron S, D Coates T, et al. American Society of Hematology 2019 guidelines for sickle cell disease: cardiopulmonary and kidney disease. Blood Adv. 2019 Dec 10;3(23):3867-3897. doi: 10.1182/bloodadvances.2019000916. PMID: 31794601; PMCID: PMC6963257.
16. Chou ST, Alsawas M, Fasano RM, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. Blood Adv. 2020 Jan 28;4(2):327-355. doi: 10.1182/bloodadvances.2019001143. PMID: 31985807; PMCID: PMC6988392.
17. DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. Blood Adv. 2020 Apr 28;4(8):1554-1588. doi: 10.1182/bloodadvances.2019001142. PMID: 32298430; PMCID: PMC7189278.
18. Kanter J, Liem RI, Bernaudin F, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. Blood Adv. 2021 Sep 28;5(18):3668-3689. doi: 10.1182/bloodadvances.2021004394C. PMID: 34581773; PMCID: PMC8945587.
19. Beaudoin F, Nikitin D, Campbell J, et al. Gene Therapies for Sickle Cell Disease – Evidence Report. Institute for Clinical and Economic Research. July 13, 2023