

Internal Pharmacy Prior Authorization Criteria

Applicable Plans:

Banner Medicare Advantage Dual HMO D-SNP (Banner Dual)

Banner Medicare Advantage Prime HMO (Banner Prime)

Guidelines for the following medications:

- **PH001: Etranacogene dezaparvovec-drlb (Hemgenix)**
- **PH002: Fidanacogene Elaparvovec (Beqvez)**
- **PH003: Elivaldogene autotemcel (Skysona)**
- **PH004: Valoctocogene roxaparvovec (Roctavian)**
- **PH005: Exagamglogene autotemcel (Casgevy)**
- **PH006: Lovotibeglogene autotemcel (Lyfgenia)**
- **PH007: Guselkumab (Tremfya)**
- **PH008: Botox (OnabotulinumtoxinA) use above 400 units/3 months**

As National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) become available for these medications, these policies will be retired, and NCDs/LCDs will be followed.

PH001: Banner MA Internal Prior Authorization Criteria- Etranacogene dezaparvovec-drlb (Hemgenix) Guideline

Effective Date: 4/1/2023

Date(s) of Review and Revision: 9/11/2024; 11/12/2025

APPLICABLE AGENT(S):

- o Etranacogene dezaparvovec-drlb (Hemgenix)

CRITERIA FOR INITIAL AUTHORIZATION:

1. Member is 18 years or older with Hemophilia B (congenital Factor IX deficiency) who has FDA approved indication of:
 - a. Currently using Factor IX prophylaxis therapy and is stable on it for at least 2 months and has received at least 150 exposure days, or
 - b. Has current or historical life-threatening hemorrhage, or
 - c. Has repeated, serious spontaneous bleeding episodesAND
2. Has not received prior treatment with any gene therapy for hemophilia B
AND
3. AAV5 Neutralizing Antibody test processing conducted with CSL Behring and documentation provided to demonstrate the patient does not have anti-AAV antibody (eg AAV-5) titers exceeding 1:678)
AND
4. Must not have history of inhibitors to Factor IX or a positive inhibitor screen as defined as greater than or equal to 0.6 Bethesda units (BU) prior to administration of Hemgenix
AND
5. Prescribed by hematologist
AND
6. Member must not have active hepatitis C infection, an active HIV infection or decompensated cirrhosis. Documentation of liver health assessments including enzyme testing [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin]
AND
7. Member will have close monitoring of transaminase levels once per week for 3 months after Hemgenix administration to mitigate the risk of potential hepatotoxicity
AND
8. Send to medical director for review and MRIoA for review

CRITERIA FOR RENEWAL:

- i. N/A. No renewal allowed. One infusion per lifetime.

INSERT QUANTITY LIMITS

1. One infusion per lifetime

LENGTH OF AUTHORIZATION:

Initial Approval Duration: 6 months

Renewal Approval Duration: N/A. No renewal allowed. One infusion per lifetime.

SOURCE OF EVIDENCE OR ADDITIONAL GUIDELINE REFERENCE:

1. Hemgenix [package insert]. King of Prussia, PA. CSL Behring LLC; November 2022.
2. HOPE-B Clinical Trial Protocol, Version 8.0 (Amendment 7.0). February 2022. Phase III trial of AMT-061 in subjects with severe or moderately severe hemophilia B. Available at https://clinicaltrials.gov/ProvidedDocs/91/NCT03569891/Prot_000.pdf.

PH002: Banner MA Internal Prior Authorization Criteria- Fidanacogene Elaparvovec-dzkt (Beqvez) Guideline

Effective Date: December 15, 2024

Date(s) of Review and Revision: 11/13/2024; 11/12/2025

CRITERIA FOR INITIAL AUTHORIZATION:

1. Member is male and 18 years or older with a diagnosis of moderate to severe Hemophilia B (congenital Factor IX deficiency) as confirmed by coagulation testing AND as documented in medical records:
 - a. Currently using Factor IX prophylaxis therapy, or
 - b. Has current or historical life-threatening hemorrhage, or
 - c. Has repeated, serious spontaneous bleeding episodes

AND

2. Has not received prior treatment with any gene therapy for hemophilia B

AND

3. Laboratory confirmation using the nAbCyte cell-based neutralizing antibody assay diagnostic, showing that the patient is negative for antibodies to AAVRh74 var (antiAAVRh74 antibodies).

AND

4. Must not have history of inhibitors to Factor IX or a positive inhibitor screen as defined as greater than or equal to 0.6 Bethesda units (BU) prior to administration of Beqvez

AND

5. Prescribed by hematologist

AND

6. Member must not have active hepatitis B or C infection, an active HIV infection with CD4 cell count ≤ 200 mm³ or viral load > 20 copies/mL, or ALT/AST/ALP > 2 times ULN, bilirubin > 1.5 times ULN, unstable liver, or biliary disease, current liver-related coagulopathy, hypoalbuminemia, persistent jaundice, cirrhosis, splenomegaly, hepatic encephalopathy, or hepatic fibrosis.

AND

7. Member will have close monitoring of ALT, AST and factor IX activity levels prior to and after therapy according to the monitoring schedule outlined in the product labeling and institute corticosteroid treatment in response to transaminase elevation and/or decrease in FIX activity after Beqvez administration to mitigate the risk of potential hepatotoxicity

AND

8. Member has been counseled on avoidance of potentially hepatotoxic substances including alcohol, which may reduce the efficacy
AND
9. Send to medical director for review and to third party reviewer for review

CRITERIA FOR RENEWAL:

- i. N/A. No renewal allowed. One infusion per lifetime.

INSERT QUANTITY LIMITS

1. One infusion per lifetime

LENGTH OF AUTHORIZATION:

Initial Approval Duration: 6 months

Renewal Approval Duration: N/A. No renewal allowed. One infusion per lifetime.

SOURCE OF EVIDENCE OR ADDITIONAL GUIDELINE REFERENCE:

1. Beqvez [package insert]. New York, NY. Pfizer Inc; April 2024.
2. Cuker, A., Kavakli, K., Frenzel, L., et. al, BENEENE-2 Trial Investigators (2024). Gene Therapy with Fidanacogene Elaparvovec in Adults with Hemophilia B. The New England journal of medicine, 391(12), 1108–1118. <https://doi.org/10.1056/NEJMoa2302982>
3. Guidelines for the Management of Hemophilia. 3rd Edition. World Federation of Hemophilia 2020. Available at: <https://www1.wfh.org/publications/files/pdf-1863.pdf>. Accessed Sep 2024.

PH003: Banner MA Internal Prior Authorization Criteria- Elivaldogene autotemcel (Skysona) Guideline

Effective Date: 5/1/23

Date(s) of Review and Revision: 9/11/24; 11/12/2025

APPLICABLE AGENT(S):

- Elivaldogene autotemcel (Skysona)

CRITERIA FOR INITIAL AUTHORIZATION:

1. Member is a male between 4 years of age and less than 18 years AND
2. Submission of medical records confirming member has a documented diagnosis of early, active cerebral adrenoleukodystrophy (CALD) AND
3. Submission of medical records documenting molecular genetic testing confirms mutation in the ABCD1 gene AND
4. Submission of medical records confirming ALL of the following:
 - Patient has elevated very long chain fatty acid levels
 - Loes score between 0.5 and 9 (inclusive) based on brain MRI assessment
 - Brain MRI utilized Gadolinium enhancement and demonstrated demyelinating lesions
 - Neurologic function score (NFS) less than or equal to 1
5. Member is not eligible for allogeneic hematopoietic stem cell transplant with an HLA-matched sibling donor AND
6. Submission of medical records confirming negative test result for:
 - Hepatitis B virus (HBV)
 - Hepatitis C virus (HCV)
 - Human T-lymphotropic virus 1 and 2 (HTLV-1/HTLV-2)
 - Human immunodeficiency virus (HIV) AND
7. Patient does not have CALD secondary to head trauma AND
8. Prescribed by a stem cell transplant physician or geneticist from a qualified treatment center AND
9. Patient has never received Skysona in their lifetime AND
10. Discontinue prophylactic anti-retroviral medications for at least one month prior to initiating medications for stem cell mobilization and until all cycles of apheresis are completed AND
11. If ALL of the above requirements are met, send to Medical Director for review and approval

CRITERIA FOR RENEWAL:

a. N/A

INSERT QUANTITY LIMITS

1. A Single dose of Skysona containing a minimum of 5.0×10^6 CD34+ cells/kg of body weight, in one or more infusion bags

LENGTH OF AUTHORIZATION:

- Initial Approval Duration: 6 months
- Renewal Approval Duration: N/A

SOURCE OF EVIDENCE OR ADDITIONAL GUIDELINE REFERENCE:

- Skysona [Package insert]. Somerville, MA. Bluebird Bio, Inc; September 2022.
- Elivaldogene Automecel: First Approval. Mol Diagn Ther. Nov 2021;25(6):803-809. doi: 10.1007/s40291-021-00555-1.

PH004: Banner MA Internal Prior Authorization Criteria- Valoctocogene roxaparvovec (Roctavian) Guideline

Effective Date: 11/15/23

Date(s) of Review and Revision: 9/11/24; 11/12/2025

APPLICABLE AGENT(S):

- Valoctocogene roxaparvovec (Roctavian)

CRITERIA FOR INITIAL AUTHORIZATION:

1. Member is 18 years or older with severe Hemophilia A (Congenital factor VIII deficiency; severe is defined as pre-treatment factor VIII level less than 1 IU/dL)
AND
2. The member meets both of the following (a and b).
 - a. Member has been adherent to Factor VIII prophylaxis therapy for at least 12 months and has received at least 150 exposure days
 - b. Occurrence of one or more serious spontaneous bleeding event while on routine prophylaxisAND all of the following:
3. Member has not received prior treatment with any other therapy containing an adeno-associated viral vector
4. Patient has been tested and found negative for active factor VIII inhibitors. Member's inhibitor level assay <1 Bethesda Unit (BU) on two consecutive occasions at least one week apart within the last 12 months. Patient is not receiving a bypassing agent (e.g. Feiba)
5. Member has no pre-existing antibodies to AAV5 capsid as measured by AAV5 total assay FDA-approved test.
6. Member has completed attestation of alcohol abstinence and has received abstinence education from the physician.
7. Prescribed by or in consultation with a hematologist.
8. Provider agrees to monitor the patient according to the FDA approved label. This includes factor VIII level tests, ALT monitoring, and steroid treatment as appropriate.
9. Provider must provide documentation member does not have active infections, either acute or uncontrolled chronic, known significant hepatic fibrosis (stage 3 or 4), or cirrhosis, or known hypersensitivity to mannitol.
10. Send to medical director and MRIoA for review.

CRITERIA FOR RENEWAL:

N/A. No renewal allowed. One infusion per lifetime.

INSERT QUANTITY LIMITS

Dose: 6×10^{13} vector genomes/kg as a single one-time dose per lifetime

LENGTH OF AUTHORIZATION:

- Initial Approval Duration: 6 months
- Renewal Approval Duration: N/A. No renewal allowed. One infusion per lifetime.

SOURCE OF EVIDENCE OR ADDITIONAL GUIDELINE REFERENCE:

1. Roctavian [package insert]. Novato, Ca. BioMarin Pharmaceutical Inc.; June 2023.

PH005: Banner MA Internal Prior Authorization Criteria- Exagamglogene autotemcel (Casgevy) Guideline

Effective Date: May 15, 2024

Date(s) of Review and Revision: 9/11/24; 11/12/2025

CRITERIA FOR INITIAL AUTHORIZATION FOR SICKLE CELL DISEASE:

1. Patient is at least 12 years of age AND
2. Confirmed diagnosis of severe sickle cell disease (includes $\beta\text{S}/\beta\text{S}$ or $\beta\text{S}/\beta\text{0}$ or $\beta\text{S}/\beta+$ genotype) as defined by:
 - a. Documented severe sickle cell disease genotype. Identification of significant quantities of HbS with or without additional abnormal B-globin chain variant by hemoglobin assay or
 - b. Identification of biallelic HBB pathogenic variants where at least one allele is p.Glu6Val pathogenic variant on molecular genetic testing
 - c. History of at least four severe vaso-occlusive crisis events in the previous two years while adhering to the therapy in (d and e) below. Vaso-occlusive crisis events are documented events requiring evaluation in a medical facility with a diagnosis of one or more of the following: acute chest syndrome, acute pain, acute splenic sequestration, acute hepatic sequestration, priapism lasting more than 2 hours, AND necessitates subsequent interventions including opioid pain management, non-steroidal anti-inflammatory drugs or red blood cell transfusion.
 - d. Patient has symptomatic disease despite treatment with hydroxyurea, or patient has documented intolerance to hydroxyurea.
 - e. Patient continues with symptomatic disease despite add on therapy such as Crizanlizumab or Voxelotor
3. Patient must be eligible for autologous stem cell transplant (HSCT) as per provider's assessment
4. A willing and healthy, available 10/10 human leukocyte antigen matched related donor is not available
5. Patient must not have had prior hematopoietic stem cell transplant or other gene therapies such as lovotibeglogene
6. Patient must not have clinically significant and active bacterial, viral, fungal, or parasitic infection
7. 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) per clinical guidelines before collection of cells (leukapheresis)
8. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloblative conditioning
9. Patient will be transfused prior to apheresis to a total Hemoglobin of 11 g/dL or less and a HbS level less than 30% and patient will be transfused at least 8 weeks prior to initiation of myeloblative conditioning
10. Will not be administered along with live vaccines while immunosuppressed

11. Patient does not have history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40
12. Patient will not receive therapy concomitantly with any of the following:
 - a. Iron chelators for 7 days prior to mobilization and 6 months post treatment, or 3 months post treatment for non-myelosuppressive iron chelators
 - b. Disease modifying agents for at least 8 weeks prior to mobilization
 - c. Hydroxyurea for at least 2 months prior to mobilization
 - d. Mobilization of stem cells using granulocyte colony stimulating factor (G-CSF)

CASGEVY CRITERIA FOR INITIAL AUTHORIZATION FOR BETA-THALASSEMIA

1. Patient is at least 12 years of age AND
2. Submission of medical records documenting genetic testing confirming diagnosis of β -thalassemia.
3. Diagnosis of TDT as defined by:
 - a. Documented homozygous β -thalassemia or compound heterozygous β -thalassemia including β -thalassemia/hemoglobin E (HbE).
 - b. Must not have α -thalassemia.
 - c. Must be considered transfusion dependent with a history of at least 100 mL/kg/year of packed red blood cells (pRBC) in the previous two years OR be managed under standard thalassemia guidelines with ≥ 8 transfusions of pRBCs per year in the previous two years
4. Patient is a candidate for an allogeneic hematopoietic stem cell transplantation
 - a. Must not have:
 - i. A prior hematopoietic stem cell transplant (HSCT) or currently be eligible for a HSCT with an HLA matched family donor
 1. Documentation that a suitable donor has not been identified, for example, a matched related donor or matched (HLA 8/8 or 7/8) unrelated donor.
 - ii. Clinically significant and active bacterial, viral, fungal, or parasite infection
 - iii. Presence of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus 1&2 (HIV-1 & HIV-2) per clinical guidelines before collection of cells (leukapheresis)
 - iv. Current immunodeficiency disorder or malignancy
 - v. Uncorrected bleeding disorder
 - vi. Uncontrolled seizure disorder
 - vii. Advanced liver disease defined as
 1. Alanine transferases or direct bilirubin greater than 3 times the upper limit of normal (ULN) OR

2. Baseline prothrombin time or partial thromboplastin time greater than 1.5 times the ULN suspected of arising from liver disease OR
3. Magnetic resonance imaging (MRI) of the liver demonstrating clear evidence of cirrhosis
4. Evidence of severe iron overload (for example, T2*-weighted magnetic resonance imaging [MRI] measurements of myocardial iron greater than 10 msec)
- viii. Have not received prior treatment with any gene therapy or are being considered for treatment with any other gene therapy for beta-thalassemia.
- ix. White blood cell (WBC) count $< 3 \times 10^9/L$ or platelet count $< 50 \times 10^9/L$ not related to hypersplenism.
5. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning
6. Patient is anticipated to provide an adequate number of cells to meet the minimum recommended dose of 3×10^6 CD34+ cells/kg.
7. Patient will be transfused to maintain hemoglobin (Hb) ≥ 11 g/dL for 60 days prior to myeloablative conditioning.
8. Prescribed by hematologist/oncologist at a treatment center with expertise in gene therapy.
9. Will not be administered along with live vaccines while immunocompromised
10. Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40
11. Patient will not receive therapy concomitantly with any of the following:
 - a. Iron chelators for 7 days prior to mobilization and 6 months post treatment, or 3 months post treatment for non-myelosuppressive iron chelators
 - b. Disease modifying agents for at least 8 weeks prior to mobilization
 - c. Hydroxyurea for at least 2 months prior to mobilization
 - d. Mobilization for stem cells using granulocyte colony stimulating factor (G-CSF)

CRITERIA FOR RENEWAL:

- i. N/A. No renewal allowed. One infusion per lifetime.

INSERT QUANTITY LIMITS

1. A single dose infusion containing 3.0×10^6 CD34+ cells/kg of body weight per lifetime

LENGTH OF AUTHORIZATION:

- Initial Approval Duration: 6 months
- Renewal Approval Duration: N/A. No renewal allowed. One infusion per lifetime

REFERENCES:

Casgevy (Package insert). Boston, MA; Vetex Inc.; December 2023. Accessed March 2024. CTG Labs – NCBI. (n.d.). <https://clinicaltrials.gov/study/NCT03655678>

PH006: Banner MA Internal Prior Authorization Criteria- Lovotibeglogene autotemcel (Lyfgenia) Guideline

Effective Date: May 15, 2024

Date(s) of Review and Revision: 9/11/2024; 11/12/2025

CRITERIA FOR INITIAL AUTHORIZATION:

Patient meets the following:

1. Patient is at least 12 years of age and not older than 50 years of age AND
2. Confirmed diagnosis of severe sickle cell disease (includes β^S/β^S or β^S/β^0 or β^S/β^+ genotype) as defined by:
 - a. Documented severe sickle cell disease genotype. Identification of significant quantities of HbS with or without additional abnormal B-globin chain variant by hemoglobin assay or
 - b. Identification of biallelic HBB pathogenic variants where at least one allele is p.Glu6Val pathogenic variant on molecular genetic testing
 - c. Patient does not have disease with more than two alpha globin gene deletions
 - d. History of at four severe vaso-occlusive crisis events in the previous two years while adhering to the therapy in (e and f) below. Vaso-occlusive crisis events are documented events requiring evaluation in a medical facility with a diagnosis of one or more of the following: acute chest syndrome, acute pain, acute splenic sequestration, acute hepatic sequestration, priapism lasting more than 2 hours, AND necessitates subsequent interventions including opioid pain management, non-steroidal anti-inflammatory drugs or red blood cell transfusion.
 - e. Patient has symptomatic disease despite treatment with hydroxyurea, or patient has documented intolerance to hydroxyurea.
 - f. Patient continues with symptomatic disease despite add on therapy such as Crizanlizumab or Voxelotor
3. Patient must be eligible for autologous stem cell transplant (HSCT) as per provider's assessment
4. A willing and healthy, available 10/10 human leukocyte antigen matched related donor is not available
5. Patient must not have had prior hematopoietic stem cell transplant or other gene therapies such as exagamglogene autotemcel
6. Patient must not have clinically significant and active bacterial, viral, fungal, or parasitic infection
7. 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) per clinical guidelines before collection of cells (leukapheresis)
8. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloblative conditioning

9. Patient will be monitored for hematologic malignancies periodically after treatment
10. Patient will be transfused at least twice, once per month, prior to apheresis to a total Hemoglobin of 8-10 g/dL (less than 12 g/dl) and a HbS level less than 30%
11. Will not be administered along with live vaccines while immunosuppressed
12. Patient does not have history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40
13. Patient will not receive therapy concomitantly with any of the following:
 - a. Iron chelators for 7 days prior to mobilization and 6 months post treatment
 - b. Disease modifying agents for at least 8 weeks prior to mobilization
 - c. Hydroxyurea for at least 2 months prior to mobilization
 - d. Mobilization of stem cells using granulocyte colony stimulating factor (G-CSF)
 - e. Prophylactic HIV anti-retroviral therapy for at least one month prior to mobilization and until all cycles of apheresis are completed
 - f. Erythropoietin for at least 2 months prior to mobilization
14. Patient does not have advanced liver disease, defined as:
 - i. Persistent aspartate transaminase, alanine transaminase, or direct bilirubin value $>3\times$ the upper limit of normal (ULN), or
 - ii. Baseline prothrombin time or partial thromboplastin time $>1.5\times$ ULN, suspected of arising from liver disease, or
 - iii. Magnetic Resonance Imaging (MRI) of the liver demonstrating clear evidence of cirrhosis, or MRI findings suggestive of active hepatitis, significant fibrosis, or inconclusive evidence of cirrhosis.
15. Patient does not have immediate family member with a known or suspected Familial Cancer Syndrome.

CRITERIA FOR RENEWAL:

- i. N/A. No renewal allowed. One infusion per lifetime.

INSERT QUANTITY LIMITS

1. A single dose infusion containing 3.0×10^6 CD34+ cells/kg of body weight per lifetime

LENGTH OF AUTHORIZATION:

- Initial Approval Duration: 6 months
- Renewal Approval Duration: N/A. No renewal allowed. One infusion per lifetime

PH007: Guselkumab (Tremfya)

Effective Date: November 20, 2025

Date(s) of Review and Revision: 11/12/2025

CRITERIA FOR INITIAL AUTHORIZATION:

Patient meets the following:

1. No serious infection AND
No concurrent administration of a live vaccine AND
No untreated latent or active tuberculosis AND

One of the following diagnoses:

Crohn's disease

1. Documented diagnosis of Crohn's disease AND
2. Patient is 18 years of age or older AND
3. Prescribed by or in consultation with a gastroenterologist

OR

Plaque Psoriasis, Psoriatic Arthritis

1. Documented diagnosis of one (1) of the following:
 - a. Moderate to severe plaque psoriasis
 - b. Active psoriatic arthritis AND
2. Patient is 6 years of age or older who also weighs at least 40kg AND
3. Prescribed by or in consultation with a rheumatologist or dermatologist

OR

Ulcerative Colitis

1. Documented diagnosis of moderate to severe ulcerative colitis AND
2. Patient is 18 years of age or older AND
3. Prescribed by or in consultation with a gastroenterologist

CRITERIA FOR RENEWAL:

Member tolerating medication and having positive results

LENGTH OF AUTHORIZATION:

12 months

PH008: Banner MA Internal Prior Authorization Criteria- Botox (OnabotulinumtoxinA) use above 400units/3-month Guideline

Effective Date: June 1, 2025

Date(s) of Review and Revision: 4/9/2025; 11/12/2025

Botox (OnabotulinumtoxinA) use above 400units/3months may be considered medically necessary for the treatment of spasticity related to neurological disease when ALL of the following criteria are met:

1. Diagnosis:

- The patient has a documented diagnosis of spasticity associated with one of the following neurological conditions, including but not limited to:
 - Stroke
 - Multiple Sclerosis (MS)
 - Cerebral Palsy (CP)
 - Traumatic Brain Injury (TBI)
 - Spinal Cord Injury (SCI)
 - Other related neurological disorders

2. Functional Impairment:

- The spasticity results in significant functional impairment or pain that affects activities of daily living (ADLs) or mobility.

3. Conservative Treatment:

- The patient has had conservative management with PT and/or OT, splinting, bracing, medications, etc. with insufficient benefit to resolve functional impairment.

4. Previous Botox Use:

- If applicable, the patient has demonstrated a positive response to prior Botox injections with documented improvement in muscle tone, function, or pain management.

5. Dose Justification:

- Up to 600 units per treatment session may be authorized if all the following are met:
 - The patient has severe spasticity involving multiple muscle groups.
 - The standard 400-unit dose was insufficient to achieve adequate symptom relief.
 - A specialist (e.g., neurologist, physiatrist) has provided clinical justification for higher doses based on individual patient needs.

6. Frequency of Treatment:

- Repeat treatment may be authorized at intervals of at least 12 weeks if there is documented evidence of continued benefit and absence of significant adverse effects.

SOURCE OF EVIDENCE OR ADDITIONAL GUIDELINE REFERENCE:

1. Tremfya [Package Insert]. Horsham, PA. Janssen Biotech, Inc; 2025.
2. Lyfgenia (lovotibeglogene autotemcel) [PACKAGE INSERT]. Somerville, MA: Bluebird. Dec 2023.
3. CTG Labs - NCBI. (n.d.). <https://clinicaltrials.gov/study/NCT02140554>
4. Evidence-Based Management of Sickle Cell Disease. Expert Panel Report, 2014. US Department of Health and Human Services National Institute of Health. Accessed January 2024.
<http://www.nhlbi.nih.gov/guidelines>
5. Frangoul H, Altshuler D, Cappellini D, et al. CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β -Thalassemia. Jan 21, 2021 N Engl J Med 2021; 384:252-260 DOI: 10.1056/NEJMoa2031054.
6. 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.
7. Ataga LK, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease and cystic fibrosis and factors associated with research productivity. JAMA Netw Open. 2020; 3(3):e201737.
8. Charache, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. N Engl J Med. 1995;332:1317-1322.
9. Kavanagh PL, Sprinz PG, Vinci SR, Bauchner H, Wang CJ. Management of children with sickle cell disease: a comprehensive review of the literature. Pediatrics. 2011;128(6):e1552-74.
10. Tremfya [Package Insert]. Horsham, PA. Janssen Biotech, Inc; 2025.
11. Intiso D, Simone V, Bartolo M et. Al. High Dosage Botulinum Toxin Type A in Subjects with Spasticity Following Acquired Central Nervous System Damage: Where are we at? Toxins. 2020 May 10;12(5):315.