Medicare Advantage Medical Benefit Drug Policy

Medical benefit drug policies are a source for Blue Cross and Blue Shield of Nebraska Medicare Advantage medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/08/2023

Hemgenix® (etranacogene dezaparvovec-drlb)

HCPCS: J1411

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of moderate to severe hemophilia B
   c. Prescribed by or in consultation with a hematologist providing attestation of knowledge the patient is suitable for treatment, including the AAV5 viral vector antibody titer
   d. Must currently be on factor IX therapy with greater than 150 prior exposure days to treatment
   e. Must not have a history of inhibitors to factor IX or a positive inhibitor screen defined as greater than or equal to 0.3 Bethesda units prior to administration of Hemgenix
   f. Must not have received prior treatment with any gene therapy for hemophilia B or are being considered for treatment with any other gene therapy for hemophilia B
   g. Must be being treated at a federally recognized hemophilia treatment center site
   h. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in the BCBSNE MA Part B drugs prior authorization list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Hemgenix is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with hemophilia B who currently use factor IX prophylaxis therapy, or have a current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

- Hemophilia B is a rare genetic bleeding disorder in which affected individuals have insufficient levels of factor IX. It is the second most common type of hemophilia and caused by mutations in the F9 gene. The F9 gene is located on the X chromosome and thus the disease is inherited as an X-linked recessive trait. About 30% of cases are the result of spontaneous genetic mutations. Studies report that over 50% of people newly diagnosed with severe hemophilia have no prior family history. Overall incidence is estimated at 1 in 25,000 male births.

- The symptoms and severity of hemophilia B may vary greatly from one person to another. Hemophilia B can range from mild to moderate to severe.

    - Mild hemophilia patients have a factor activity of 5% to 40% and usually do not experience any major problems in everyday life. It often goes unnoticed until puberty or adulthood when bleeding after surgery or a deep cut lasts longer than normal. These patients do not typically need prophylactic therapy and only require on-demand factor for injuries or surgeries.

    - Moderate hemophilia patients have a factor activity of 1% to 5% and may have occasional episodes of spontaneous bleeding from deep tissues such as joints and muscles. These episodes are usually associated with some injury or inciting event. Individuals with moderate hemophilia B are at risk for prolonged bleeding following surgery or trauma. Affected individuals are usually diagnosed by 5 or 6 years of age. The frequency of spontaneous bleeding episodes in individuals with moderate hemophilia B is highly variable resulting in some patients needing consistent prophylactic factor IX and others only needing on-demand factor IX for medical procedures.

    - Severe hemophilia patients have a factor level of less than 1% and often have bleeding for no known reason, especially in the joints and muscles. From infancy, patients bruise easily and as they become more active, learn to walk, and put more strain on their joints and muscles, bleeding starts to occur. Without preventative treatment, a young child may experience 2 to 5 spontaneous bleeding episodes per month.

- Hemophilia B should be suspected in individuals presenting with a history of easy bruising, spontaneous bleeding, particularly into the joints, muscles, and soft tissues, or excessive bleeding following trauma or surgery. If hemophilia is suspected, the clinician should obtain the patient's bleeding history and family history of abnormal or unexplained bleeding experienced by any siblings or maternal male relatives to assess patterns of inheritance and assist with diagnosis. A definitive hemophilia B diagnosis is based on a factor assay to demonstrate a deficiency of factor IX. Once an individual is diagnosed with hemophilia B, the specific mutation in the F9 gene responsible for causing hemophilia may be identified.

- The current standard of care for hemophilia B is the use of factor IX replacement therapy. There are two types of factor products available to treat hemophilia which include plasma derived factor, entirely made of plasma from human donations and recombinant factor, which is made by genetically engineered technology, both with standard and extended half-life products. All factor products have demonstrated to have similar safety and efficacy in clinical studies treating or reducing bleeding episodes with the apparent difference in the frequency of administration: up to three times weekly injections for standard products and weekly or every two weeks for extended half-life products. To be enrolled in the HOPE-B trial, patients needed to be stable on factor IX therapy for 6 months prior Hemgenix administration.

- It is estimated that less than 5% of individuals with severe hemophilia B develop inhibitors against factor IX replacement therapy. Inhibitors most often develop during childhood, especially during the first 20 exposure days. Exposure days are counted as a day during which a patient receives factor. Controlling bleeds is a greater challenge in hemophilia patients with inhibitors than in those without. Inhibitors to factor IX are associated with a higher disease burden, including increased risk of musculoskeletal complications, pain, physical limitations, and treatment challenges, all of which may impact a patient's physical functioning, capacity for physical activities, and quality of life. The definition of a positive inhibitor is a Bethesda titer of greater than or equal to 0.3 BU for factor IX. Patients positive for factor IX inhibitors or with a prior history of factor IX inhibitors were excluded from the HOPE-B trial. In order to limit the risk of inhibitor development following Hemgenix therapy, the HOPE-B study also required patients had greater than 150 prior exposure days to factor IX therapy before receiving gene therapy.

- Hemgenix uses an adeno-associated virus serotype 5 vector (AAV5) to deliver a functional copy of the F9 gene to the patient's liver where functional factor IX is produced. Patients with high AAV5 antibody titers may not respond to gene therapy due to the antibodies neutralizing Hemgenix before the functional F9 gene can be properly incorporated into the patient's genome. The HOPE-B study did not exclude patients from the trial based on antibody titers, however, the trial had one non-responder to treatment whose antibody titer level was 1:700. It is important for physicians to be aware of the patients antibody titer levels before administering treatment.

References:

1. Hemgenix [prescribing information]. King of Prussia, PA: CSL Behring LLC; November 2022.
2. Clinicaltrials.gov. HOPE-B: Trial of AMT-061 in severe or moderately severe hemophilia b patients (NCT03569891). Available at: https://clinicaltrials.gov/ct2/show/NCT03569891. Accessed on November 22, 2022.
3. Shapiro AD. Hemophilia b. 2018. Available at: https://rarediseases.org/rare-diseases/hemophilia-b/. Accessed on November 22, 2022.
4. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 2020 August 3. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046. Accessed on: November 22, 2022.
5. Carcao M and Goudemand J. Inhibitors in hemophilia: a primer. 2018 Nov. Available at: https://www1.wfh.org/publication/files/pdf-1122.pdf. Accessed on November 22, 2022.

Policy History		
#	Date	Change Description
1.2	Effective Date: 06/08/2023	Removed confirmation of diagnosis via decreased factor IX levels
1.1	Effective Date: 02/02/2023	New policy
1.0	Effective Date: 10/06/2022	Preliminary drug review

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*