- 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.

- The Audaire Health platform is a provider portal that is used to capture clinical outcome information for patients on select high-cost treatments, such as gene and cellular therapies. If a patient meets medical necessity as defined by this policy and is approved for treatment, the requesting physician must attest to providing clinical outcome information within the Audaire Health™ provider portal at the requested cadence.

References:

1. Hemgenix [prescribing information]. King of Prussia, PA: CSL Behring LLC; November 2022.
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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
1.1	Effective Date: 02/02/2023	New policy
1.0	Effective Date: 12/05/2022	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.*