Molina Clinical Policy
Hemgenix (etranacogene dezaparvovec-drlb): Policy No. 429

Last Approval: 1/4/2023
Next Review Due By: December 2023

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

Hemophilia is typically an inherited bleeding disorder caused by deficiency of coagulation factor VIII (hemophilia A), factor IX (hemophilia B), or factor XI (hemophilia C). Rare cases are acquired later in life. Hemophilia A and B are X-linked recessive bleeding disorders, while Hemophilia C follows an autosomal recessive inheritance pattern. The genetic mutation is found on chromosome 4. In the United States, approximately 30,000 to 33,000 people have hemophilia, with Hemophilia A being four times as common as hemophilia B. Hemophilia A has an incidence of one in 5,000 male live births compared to one in 30,000 for hemophilia B (CDC, 2022). Hemophilia B represents an estimated 15% of hemophilia patients (FDA, 2022). Hemarthrosis, the hallmark of severe hemophilia, is the major cause of serious bleeding events, disability, and reduced quality of life in patients with factor VIII or factor IX deficiency. Repeated hemarthrosis frequently results in hemophilic arthropathy, which is characterized by cartilage and bone degradation, bone remodeling, and progressive loss of function.

Hemophilia B (Christmas Disease) a deficiency in Factor IX clotting activity, results in spontaneous bleeding in the absence of recognized trauma and delayed or recurrent bleeding prior to complete wound healing (Shah et al., 2022). Factor levels (an individual's percentage of factor IX) have traditionally been used to assess the severity of hemophilia B. Although severity based on factor levels does not perfectly correlate with clinical severity in any individual, no other classification system is widely accepted. Severe disease is defined by factor levels that are less than 1% of normal, according to factor level classifications (Refer to 'Supplemental Information' section for additional information on severity). In severe disease, recurrent bleeds typically result in arthropathy, joint contractures, and pseudotumors, resulting in chronic pain, disability, and a diminished quality of life. The current standard of care is Factor IX replacement therapy, with moderate to severe hemophilia B patients receiving prophylactic infusions of Factor IX. Gene therapy for the treatment of hemophilia B aims to alter the clinical phenotype of hemophilia to a milder form or cure by increasing endogenous coagulation factor levels via the transfer of a functional gene encoding for the respective deficient coagulation factor and subsequent transgene expression. In the absence of longer-term data, however, the efficacy and durability of gene therapy as a new treatment method for a cure or permanent physiologic recovery remain unknown.

Hemgenix (etranacogene dezaparvovec-drlb, or etrana-dez; formerly AMT-061) is an adeno-associated virus serotype 5 (AAV5)-mediated gene therapy for hemophilia B. It is a single intravenous infusion of the highly active Padua variant of the gene for Factor IX to cells in the liver, resulting in production of an active variant of Factor IX. Hemgenix is indicated for the treatment of hemophilia B in adults who currently use Factor IX prophylaxis therapy, have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes. Patients undergoing gene therapy will still require on-demand factor therapy, which should be accessible in cases such as trauma, surgery, and spontaneous bleeding. FDA approval in November 2022 was based on an 18-month interim analysis of data from the HOPE-B trial, a Phase 3, open-label, single-dose, multi-center, multinational trial. A total of 54 of the 67 enrolled adult males with severe or moderately severe hemophilia B were dosed with etrana-dez and were included in the analysis (NCT03569891). Patients were initially enrolled in a 6-month observational period during which they continued to receive current standard of care and recorded use of Factor IX replacement therapy and bleeding episodes. After the lead-in period, patients received a single intravenous dose of AMT-061. The FDA labeling (2022) reported efficacy data up to 18 months post treatment; 53 of the 54 dosed completed the

18-month follow-up. One patient died from urosepsis, and another patient developed hepatocellular cancer, but both were assessed as not related to the study treatment.

Long-term durability of clinical benefit and safety of gene therapy for hemophilia remains unknown, in addition to the uncertainty of the long-term net benefits of Hemgenix compared with Factor IX prophylaxis. Potential safety issues of concern include genotoxicity, protein overexpression, immunotoxicity, insertional mutagenesis in reproductive cells could lead to infertility or, indirectly, to birth defects, and horizontal and vertical transmission (Batty and Lillicrap 2021). There are also uncertainties about the long-term impact of the therapy on liver function and the risk for hepatocellular carcinoma due to the integration of liver-targeting AAV vector DNA into the genome which carries the theoretical risk of hepatocellular carcinoma development(ICER, 2022). Longer follow-up is required to fully assess the benefits and potential risks of these treatments.

COVERAGE POLICY

Hemgenix (etrana-dez) for the treatment of hemophilia B may be considered medically necessary when **ALL** of the following criteria with are met with relevant documentation:

1. A diagnosis of hemophilia B in an adult (age 18 and older) male; **AND**
2. Severe hemophilia B defined by Factor IX baseline residual level less than or equal to 1 IU/dL; **AND**
3. Member is on Factor IX prophylaxis with a minimum of 150 exposure days to factor replacement; **AND**
4. Member has not received, or is being considered for other gene therapy, or investigational cellular therapy for hemophilia; **AND**
5. No presence or history of Factor IX inhibitors (Factor IX inhibitor titer test results required).
   NOTE: The definition of a positive inhibitor is a Bethesda titer of ≥0.3 BU for Factor IX (World Federation of Hemophilia Guidelines, 3rd edition); **AND**
6. HIV
   a. Member is HIV negative documented by lab test within the past 3 months, OR
   b. HIV positive AND well-controlled on antiretroviral therapy; **AND**
7. Hepatitis B and C:
   a. Member does NOT have an active infection with hepatitis B or C virus documented by lab tests within the past 3 months:
      - Negative hepatitis B surface antigen, and
      - Negative hepatitis C virus (HCV) antibody, OR HCV antibody is positive AND HCV RNA is negative
   b. For members with a history of hepatitis B or C exposure: Member is NOT currently using antiviral therapy for hepatitis B or C.

LIMITATIONS AND EXCLUSIONS

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

The following are considered **exclusions** based on insufficient evidence:

1. Prior treatment with Hemgenix or other gene therapy for hemophilia, or being considered for treatment with other gene therapy; AND
2. Current participation, or anticipated participation in any interventional clinical trial involving drugs or devices within one year of Hemgenix therapy; AND
3. Positive Factor IX inhibitor test, or history of Factor IX inhibitors; AND
4. Positive for HIV and not controlled with anti-viral therapy; AND
5. Hepatic impairment or disease, defined by ANY of the following:
   - Advanced hepatic impairment (e.g., cirrhosis, advanced liver fibrosis); or
   - Active, uncontrolled Hepatitis B or C; or

- Alanine transaminase at least 3 times the upper limit of normal; or
- Alkaline phosphatase at least 3 times the upper limit of normal; or
- Bilirubin at least 3 times the upper limit of normal.

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

1. Any indications other than those listed above
2. Any criterion listed above that is not met by the member or that is submitted without the required supporting documentation.

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

PRESCRIBER REQUIREMENTS: Prescribed by a board-certified hematologist in coordination with a Hemophilia Treatment Center for administration.

AGE RESTRICTIONS: Age ≥18 years at the time of infusion

GENDER RESTRICTIONS: Male

DOSING CONSIDERATIONS: Recommended dose is 2 x 10^{13} genome copies (gc) per kg of body weight as a one-time IV infusion.

MONITORING PARAMETERS: Member should be monitored according to FDA-approved labeling and best practice.

QUANTITY LIMITATIONS: ONE (1) treatment course of Hemgenix per lifetime. Additional infusions will not be authorized.

ADMINISTRATION: Hemgenix is considered a provider-administered therapy in a Hemophilia Treatment Center by a physician(s) with experience in the treatment of patients with hemophilia B.

CONTINUATION OF THERAPY: Not applicable as this is a one-time therapy. Reauthorization requests or requests for additional therapy beyond a single dose are considered experimental and will not be authorized.

The safety and efficacy of repeat treatment has not been studied and is currently not supported by any compendia nor indicated in the current FDA approved labeling. Repeat administration of 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 Hemgenix. The evidence is insufficient to determine the effects on net health outcomes.

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.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: Intravenous Infusion

DRUG CLASS: Antihemophilic Agent; Gene Therapy, Adeno-Associated Virus

FDA-APPROVED USES: Hemophilia B
Treatment of hemophilia B (congenital factor IX deficiency) in adults who currently use Factor IX prophylaxis therapy, have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.
FDA approval: November 22, 2022
Designations: Orphan Drug (2019) and Fast Track Designations (2019)

COMPENDIAL APPROVED OFF-LABELED USES: None

SUMMARY OF MEDICAL EVIDENCE

The Biologics License Application (BLA) for etrana-dez is supported by results from the Phase 2 AMT-061-01 (NCT03489291) and the pivotal HOPE-B trial (NCT03569891). Both are single-arm trials that included adult males with moderately severe to severe hemophilia B. The annualized bleeding rate (ABR) at 52 weeks was assessed as a primary outcome in the HOPE-B trial, while factor IX activity was considered a primary outcome for the Phase 2b trial. The patients in these two trials received a single dose of etrana-dez 2 x 10^{13} gc/kg.

Pivotal Phase 3 Trial

The effectiveness was determined by reductions in the ABR of adult males. The trial reported achievement in increased Factor IX activity levels, a decreased need for routine Factor IX replacement prophylaxis, and a 54% reduction in ABR relative to baseline. The ABR for all bleeds after stable factor IX expression, assessed at 18 months, was reduced by 54% and 94% of patients treated with Hemgenix discontinued use of prophylaxis and remained free of previous continuous routine prophylaxis therapy.

Inclusion criteria included males, at least 18 years old, diagnosis of severe or moderately severe congenital hemophilia B, currently on factor IX prophylaxis and exposure to Factor IX protein for at least the past 150 days. Key exclusion criteria included a history of Factor IX inhibitors or a positive Factor IX inhibitor test at screening, select liver screening laboratory test values over 2 times the upper limit of normal or history of hepatitis B or C or active infection (given the risk of potential hepatotoxicity), a positive HIV test that is not controlled with antiviral therapy, and previous gene therapy treatment.

HOPE-B (Health Outcomes with Padua gene: Evaluation in Hemophilia B; NCT03569891). The pivotal Phase 3 HOPE-B trial is an **ongoing,** single-arm, open-label multinational study to assess the safety and effectiveness of Hemgenix (n=54). Adult males with moderately severe to severe hemophilia B requiring prophylactic Factor IX replacement therapy were enrolled in a prospective, ≥6 month observational period during which they continued to use their current standard of care therapy to establish an ABR baseline. After a 6-month lead-in, 54 patients received a single intravenous infusion of Hemgenix at a dose of 2 x 10^{13} gc/kg and 53 participants completed at least 18 months of follow-up. The primary outcome was ABR at 52 weeks.

Annualized Bleeding Rates

Bleed Type	**Relative Risk Reduction*** **Comparing ABR following gene therapy to the ABR for the same participants on factor prophylaxis prior to gene therapy*
Treated Joint Bleeds	80%
Treated Bleeds	77%
All Bleeds	64%

All reductions were clinically and statistically significant. Patients treated with etrana-dez had an 80% reduction in treated joint bleeds and similar reductions in other bleeds when compared with their bleeding rates on factor prophylaxis prior to gene therapy. The trial met its primary endpoint of reduction in ABR post-treatment compared with baseline Factor IX prophylactic therapy. The 52-week adjusted ABR for all bleeds was reduced by 64% (P = 0.0002) from 4.19 during the 6-month lead-in period to 1.51 during months 7 to 18.

- 7 to 18 months post-infusion, the mean adjusted ABR for all bleeds was reduced by 54% compared to the six-month lead-in period on Factor IX prophylactic replacement therapy (4.1 to 1.9).
- Results indicate that Hemgenix produced mean Factor IX activity of 39.0 IU/dL (range: 8.2-97.1) at 6 months, 41.5 (range 5.9-113) at 12 months, and 36.9 IU/dL (range: 4.5-122.9) at 18 months post-treatment. *While none of the responders resumed factor prophylaxis during the trial's 18-month duration, the long-term outcomes are unknown. At 18 months, the levels were marginally lower than at 6 and 12 months. It remains to be established if the lowering trend persists over time or if the levels of factor expression remain steady after numerous years of follow-up.*
- It should also be noted that at 6 months after gene therapy, factor levels ranged from 8.2 to 97.1 IU/dL, demonstrating a wide range of clinical response and variability.
- In addition, 94% of study participants (51 out of 54) who received Hemgenix discontinued use of prophylaxis and remained free of previous continuous routine prophylaxis therapy (Prescribing Information, 2022). Two

participants were unable to stop routine prophylaxis after gene therapy treatment: one had high antibody titers to the adenoassociated virus vector at baseline and the second only received 10% of the target dose. The third participant stopped prophylaxis at 6 months per study protocol but received it again during days 396 to 534.

- Preexisting AAV5 NAbs were not used as an exclusion criterion. Benefits were reported regardless of the preexisting antibodies which suggests that nearly all individuals with hemophilia B may benefit from treatment.

Hemgenix was generally well-tolerated with over 80% of adverse events (AEs) considered mild. No serious AEs were reported in a safety analysis combining data from the 2 clinical studies (n=3 and n=54). The most common AEs were alanine aminotransferase (ALT) elevations (42%), aspartate aminotransferase (AST) elevations (42%), blood creatine kinase elevations (42%), infusion-related reactions (33%), headache (18%), flu-like symptoms (14%), fatigue (12%) and malaise (12%). No inhibitors to Factor IX were reported.

- One patient had a significant adverse event related to hepatocellular cancer. However, according to independent molecular characterization and vector integration study of the tumor and surrounding tissue, the hepatocellular carcinoma was not associated to Hemgenix therapy.
- According to the FDA prescribing information: *"the integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development."* While AAV is a non-integrating vector, it may integrate in small amounts into the nuclear genome; the long-term clinical implications and risk of cancer are unknown.

Limitations of the study include an uncontrolled design with no comparison to individuals receiving factor replacement therapy and a relatively small sample size, as well as the inability to confirm the long-term durability of this single dose. It should also be noted that not all individuals were able to stop prophylaxis after treatment and one out of the 54 participants resumed prophylaxis use after stopping for approximately 6 months, suggesting there may be variable efficacy and a possible waning effect of the treatment. Additional long-term data is needed to establish the durability of Hemgenix in reducing bleeding and long-term complications, particularly as compared to standard of care factor replacement therapy (including Factor IX preparations with longer half-lives).

HOPE-B is expected to conclude in **March 2025.**

Post-Marketing Study
With the BLA approval, the FDA required a post-marketing study to assess the correlation between the serious risk of bleeding associated with the failure of the expected pharmacological action of Hemgenix and pre-existing anti-AAV5 NAbs to the capsid of Hemgenix using a validated assay. The study will include at least 35 hemophilia B patients treated with Hemgenix, with at least 10 having pre-treatment anti-AAV5 NAbs titers of 1:1400 or higher. The trial will assess ABR before and after therapy, accounting for the patients' baseline ABR while receiving standard care, and an 18-month follow-up after receiving Hemgenix. The study is expected to be completed by **December 31, 2028.**

National and Specialty Organizations

World Federation of Hemophilia (WFH)
Guidelines for the Management of Hemophilia 2020, 3rd edition
The guidelines strongly advise that individuals with a severe phenotype of both hemophilia A and hemophilia B be on prophylaxis adequate to avoid all bleeding. Long-term prophylaxis is recommended as the standard of care, particularly in children, to prevent bleeding, hemarthrosis, and to improve quality of life. The prophylactic regimen should, whenever possible, be individualized for each patient based on bleeding phenotype, unique pharmacokinetics, and joint status. The guidelines do not specify a preference for recombinant over plasma-derived clotting factor concentrates and indicate that the selection between these product types should be determined based on availability, cost, and patient preferences.

For pediatric patients with severe hemophilia, WFH recommends initiating prophylaxis with clotting factor early (before age 3 and before the onset of joint disease). The dosing and interval for clotting factor prophylaxis (either standard or extended half-life) should be adequate to prevent spontaneous and breakthrough bleeding, as well as hemarthrosis. The WFH recommends escalation of prophylactic dose and orthopedic interventions in the event of a breakthrough bleed while on a prophylactic regimen.

The guidelines address gene therapy in general, noting that 'Gene therapy should make it possible for some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies. This will require evaluation through long-term follow-up as part of clinical trials and registries.' The current 2020 guidelines include no specific recommendations for etrana-dez.

A Gene Therapy Registry is being established to compile long-term data on the safety and efficacy of hemophilia patients treated with gene therapies to gain understanding and evidence about durability and variability of therapies (Konkle et al. 2021).

Institute for Clinical and Economic Review (ICER)
ICER published the Final Evidence Report assessing the comparative clinical effectiveness and value of etrana-dez (Hemgenix, CSL Behring) for hemophilia B (December 22, 2022).

ICER acknowledged from the patients' perspective that treatment with etrana-dez resulted in a significant reduction in ABRs, ranging between 64% for all bleeds to 80% for treated joint bleeds, as reported from the Phase 3 HOPE-B trial, in addition to alleviating the pain and minimizing potential disability from bleeding events. The reduction in burden of therapy from weekly or more frequent intravenous Factor IX injection was also highlighted as a significant important benefit, with 96% of the participants in the HOPE-B trial discontinuing FIX prophylaxis. Of note, 100% of the 52 patients with successful transduction during the initial 18 months of treatment were free from continuous FIX prophylaxis; none of the patients were required to resume factor prophylaxis.

The report states that while the results are encouraging, it is not yet evident if the initial elevation in factor IX levels will be sustained for decades. There is still considerable uncertainty regarding the long-term net benefits of etrana-dez in comparison to factor IX prophylaxis due to the uncontrolled study design, small number of patients studied, and relatively brief follow-up. Particularly, the long-term effects of the therapy on liver function and the risk of hepatocellular carcinoma are unknown. ICER concluded 'moderate certainty of a small or substantial health benefit with high certainty of at least a small net health benefit (B+) for etranacogene dezaparvovec compared with factor IX prophylaxis.'

SUPPLEMENTAL INFORMATION

Hemophilia B disease severity is classified as mild, moderate, or severe based on the plasma concentration of Factor IX (normal activity level 50%-150%):

- **Mild** is defined as factor IX activity > 5%-40% (> 0.05-0.4 units/mL), is usually diagnosed later in life, and is characterized by prolonged bleeding following major trauma or surgery.
- **Moderate** is defined as factor IX activity ≥1%-5% (0.01-0.05 units/mL), is usually diagnosed between age 5 and 6 years, and is characterized by bleeding following minor trauma but may present with spontaneous bleeding.
- **Severe** is defined as factor IX activity < 1% (< 0.01 units/mL), is usually diagnosed in the first 2 years of life and may present with spontaneous mild or life-threatening bleeding.

CODING & BILLING INFORMATION

CPT	Description
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)

HCPCS	Description
C9399	Unclassified drugs or biologicals (hospital outpatient use only) [when specified as Hemgenix (etranacogene dezaparvovec-drlb)]
J3590	Unclassified biologics [when specified as Hemgenix (etranacogene dezaparvovec-drlb)]

AVAILABLE DOSAGE FORMS: Suspension for IV infusion. Concentration of 1 x 10^{13} gc/mL, and each vial contains an extractable volume of not less than 10 mL. Provided as kit containing 10-48 vials; each kit constitutes a dosage unit based on patient's body weight.

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

1/4/2023 New policy. IRO Peer Review. 12/30/2022. Policy was reviewed by practicing physician board-certified in Oncology/Hematology.

REFERENCES

Government Agency

1. Centers for Medicare and Medicaid Services (CMS). Medicare Coverage Database. National coverage determination (NCD) (search: etranacogene dezaparvovec; hemophilia). Accessed at: CMS.
   - No NCD located
2. Centers for Disease Control and Prevention (CDC).
   - Hemophilia. Page reviewed: August 1, 2022. Available at CDC. Accessed December 2022.
   - A New Study of Hemophilia Occurrence Finds Many More Cases in the United States. Page reviewed: August 8, 2022. Available at CDC. Accessed December 2022.
3. ClinicalTrials.gov.
   - **NCT02396342.** Trial of AAV5-hFIX in Severe or Moderately Severe Hemophilia B. Last updated June 27, 2022. Available at: NCT02396342. Accessed December 2022
   - **NCT03489291** (Phase 2 AMT-061-01 trial). Dose Confirmation Trial of AAV5-hFIXco-Padua. Last updated June 16, 2022. Available at: NCT03489291. Accessed December 2022
   - **NCT03569891(Phase 3 HOPE-B trial)**. HOPE-B: Trial of AMT-061 in Severe or Moderately Severe Hemophilia B Patients. Last updated October 10, 2022. Available at: NCT03569891. Accessed December 2022
4. U.S. Food and Drug Administration (FDA)
   - BLA Approval. November 22, 2022. Available at: FDA. Accessed December 2022.
   - FDA approves first gene therapy to treat adults with hemophilia B [press release]. Nov. 22, 2022. Available at: FDA. Accessed Nov. 22, 2022.

Prescribing Information and Drug Compendia

1. Hemgenix (etranacogene dezaparvovec) [prescribing information]. Kankakee, IL: CSL Behring LLC; November 2022.
2. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. Available from ClinicalKey. Published 2021. Accessed December 2022. Registration and login required.

Manufacturer Publications

1. CSL Behring. FDA accepts CSL Behring's biologics license application for etranacogene dezaparvovec for priority review. 2022 May 24. Available at: CSL Behring. Accessed December 2022.

Peer Reviewed Publications

1. Pipe SW, Leebeek FWG, Recht M, et al. Adults with severe or moderately severe hemophilia B receiving Etranacogene Dezaparvovec in the HOPE-B phase 3 clinical trial continue to experience a stable increase in mean factor IX activity levels and durable hemostatic protection after 24 months' follow-up. Blood. 2022;140 (supplement 1):4910-4912. Published online November 15, 2022. doi:10.1182/blood-2022-166135.
2. Shah J, Kim H, Sivamurthy K, et al. Comprehensive analysis and prediction of long-term durability of factor IX activity following etranacogene dezaparvovec gene therapy in the treatment of hemophilia B. Curr Med Res Opin. 2022 Oct 25:1-11. doi: 10.1080/03007995.2022.2133492. Epub ahead of print. PMID: 36285399.
3. Batty P, Lillicrap D. Gene therapy for hemophilia: Current status and laboratory consequences. Int J Lab Hematol. 2021 Jul;43 Suppl 1:117-123. doi: 10.1111/ijlh.13605. PMID: 34288447.
4. Von Drygalski A, Giermasz A, Castaman G et al. Etranacogene dezaparvovec (AMT-061 phase 2b): normal/near normal FIX activity and bleed cessation in hemophilia B. Blood Adv. 2019; 3(21):3241-3247.

National and Specialty Organizations

1. Institute for Clinical and Economic Review (ICER). Tice JA, Walton S, Herce-Hagiwara B, et al. Final Evidence Report: Gene Therapy for Hemophilia B and An Update on Gene Therapy for Hemophilia A: Effectiveness and Value. Published December 22, 2022. Available at ICER. Accessed December 2022.
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- Konkle BA, Coffin D, Naccache M, et al. The world federation of hemophilia gene therapy registry. Presented at: ISTH 2021 Congress; July 17-21, 2021. Abstract PB0661.
- Srivastava A, Santagostino E, Dougall A, the WFH Guidelines for the Management of Hemophilia panelists and co-authors, et al. WFH guidelines for the management of hemophilia, 3rd edition. Haemophilia. 2020;26(S6):1–158. doi: 10.1111/hae.14046. Epub 2020 Aug 3. Erratum in: Haemophilia. 2021 Jul;27(4):699. PMID: 32744769.

Other Peer Reviewed and Professional Organization Publications (used in the development of this policy)

1. Pipe SW, Leebeek F, Recht. et al. 2141 Adults with Severe or Moderately Severe Hemophilia B Receiving Etranacogene Dezaparvovec in the HOPE-B Phase 3 Clinical Trial Continue to Experience a Stable Increase in Mean Factor IX Activity Levels and Durable Hemostatic Protection after 24 Months' Follow-up. Oral and Poster Abstracts. Session: 801. Gene Therapies: Poster I. Presented at the 64th ASH American Society of Hematology (ASH) Annual Meeting and Exposition.
2. Soucie JM, Miller CH, Dupervil B, Le B, Buckner TW. Occurrence rates of haemophilia among males in the United States based on surveillance conducted in specialized haemophilia treatment centres. Haemophilia. 2020 May;26(3):487-493. doi: 10.1111/hae.13998. Epub 2020 Apr 24. PMID: 32329553; PMCID: PMC8117262.
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   - Hoots WK and Shapiro AD. Clinical manifestations and diagnosis of hemophilia. Jan 05, 2022. Topic 1310 Version 39.0. Available at: UpToDate. Accessed December 2022.
4. [DEFINITIONS] DynaMed. Hemophilia B. EBSCO Information Services. Available at: Dynamed. Accessed December 1, 2022. Registration and login required.
5. [DEFINITIONS] Blanchette VS, Key NS, Ljung LR, Manco-Johnson MJ, van den Berg HM, Srivastava A. Definitions in hemophilia: communication from the SSC of the ISTH. J Thromb Haemost. 2014; 12(11):1935-1939. https://doi.org/10.1111/jth.12672.
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7. National Organization for Rare Disorders (NORD). Hemophilia B. Available at: NORD Accessed December 2022.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*