4-YEAR DATA UPDATE

CSL Behring

Healthcare Systems

HEMGENIX® (etranacogene dezaparvovec-drlb)

An innovative, single-dose gene therapy for hemophilia B that demonstrated cost savings for the average plan in fewer than 4 years[1,2]*

Indication

HEMGENIX is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX is for single use intravenous infusion only.

The data presented in this resource and publication are consistent with the statistical plan for the HOPE-B clinical trial. The data were evaluated independently from the HEMGENIX prescribing information and utilized a different methodology for interpreting the data. Therefore, some differences are present between the data from the published clinical trial and the data contained within the prescribing information. Please refer to the prescribing information when assessing HEMGENIX for clinical practice.

*Based on the HEMGENIX Access Decision Model (ADM). Accessed January 2025.

Please see Important Safety Information on page 9 and full prescribing information for HEMGENIX.

HEMGENIX® etranacogene dezaparvovec-drlb

The value of HEMGENIX at 4 years

At 4 years, a single dose of HEMGENIX was associated with[3]:

96%

REDUCTION IN FACTOR IX CONSUMPTION

37%

MEAN FACTOR IX ACTIVITY

61%

REDUCTION IN ANNUALIZED BLEED RATE (ABR) VS ROUTINE FACTOR IX PROPHYLAXIS*

At 4 years, HEMGENIX continues to:

- Be associated with NO serious treatment-related adverse reactions
- NOT be associated with the development of inhibitors to factor IX

*Adjusted ABR for all bleeds decreased from an average of 4.16 for prophylaxis during the lead-in period to 1.63 in months 7 to 48 after treatment, a reduction of 61%. During months 7 to 18, ABR for all bleeds decreased by 64%.

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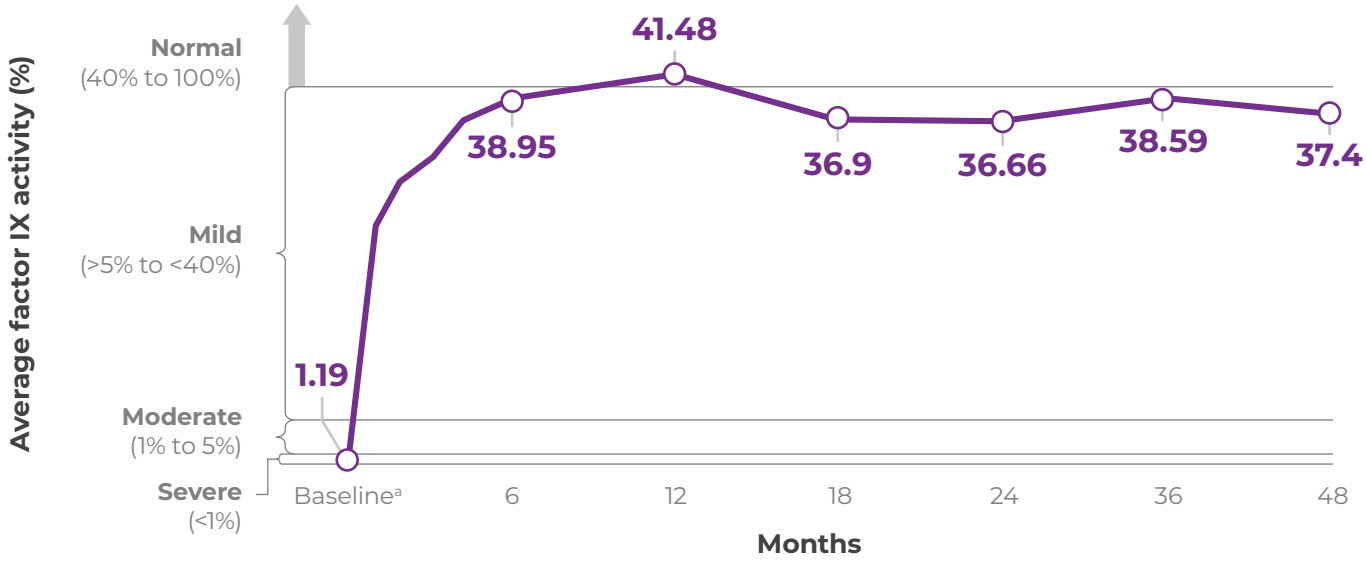
At 4 years, a single dose of HEMGENIX demonstrated sustained factor IX levels

Elevated and sustained factor IX levels for years after a single infusion[3]

Factor IX activity was sustained over 4 years after dosing[3]



A single dose of HEMGENIX resulted in mild to normal mean factor IX levels sustained over a period of

4 YEARS

[a]Baseline factor IX was imputed based on the subject's historical hemophilia B severity documented on the Case Report Form. If the subject had documented severe factor IX deficiency (factor IX plasma level <1%), their baseline factor IX activity level was imputed as 1%. If the subject had documented moderately severe factor IX deficiency (factor IX plasma level ≥1% and ≤2%), their baseline factor IX activity level was imputed as 2%. Standard error was not provided at baseline.

Uncontaminated data from the central laboratory were used; "uncontaminated" meant that the blood sampling did not occur within 5 half-lives of exogenous factor IX use. Both the date and time of exogenous factor IX use and blood sampling were considered in determining contamination. Factor IX levels beginning with the week 3 assessment were used in the analysis. All efficacy data collected after liver transplants were excluded from the analysis.

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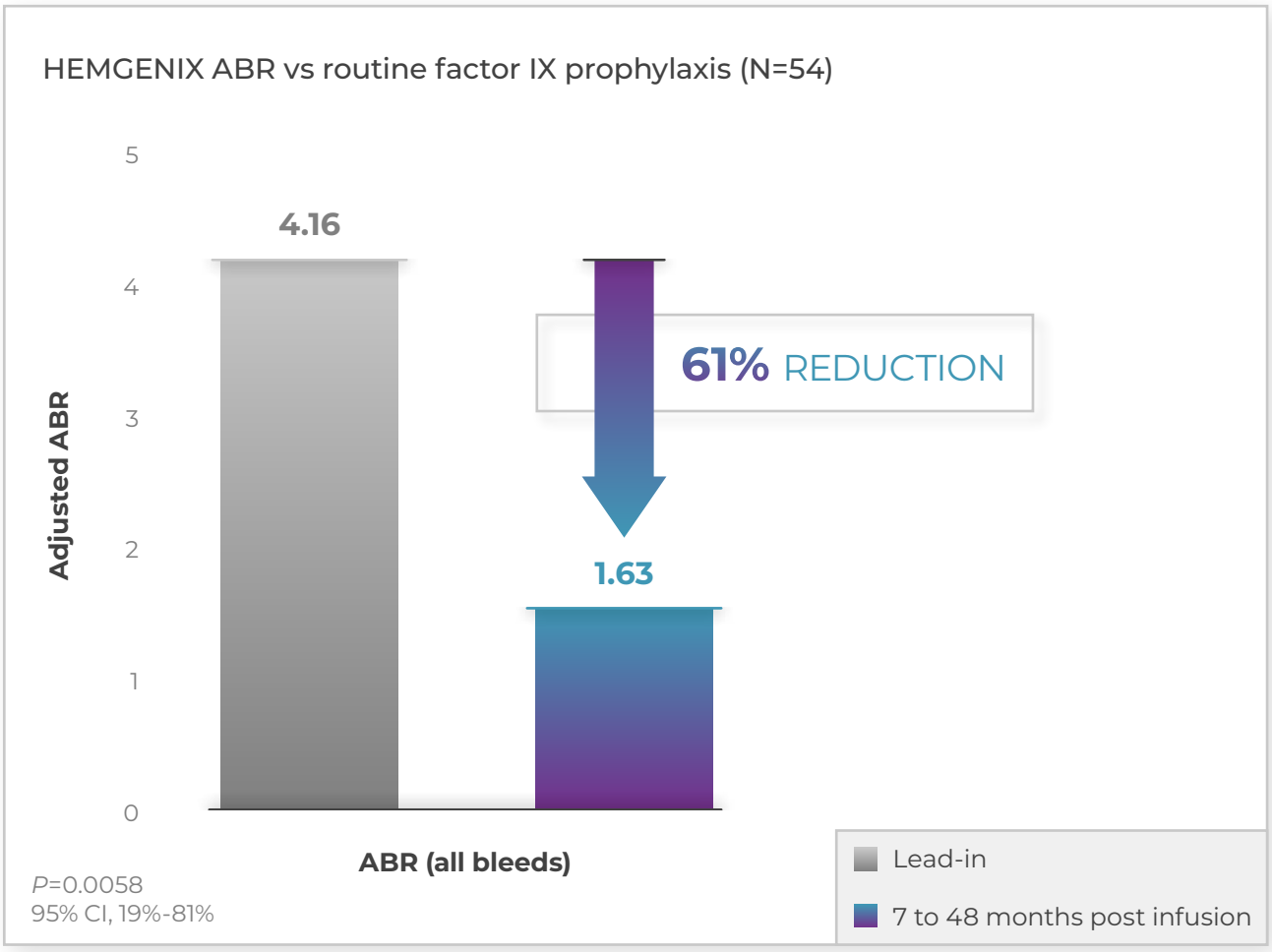
At 4 years, patients treated with HEMGENIX showed sustained ABR reductions*

A one-time infusion of HEMGENIX demonstrated noninferiority of ABR through 7 to 48 months compared with the lead-in period[3]



Adjusted ABR for all bleeds during the period between months 7 and 18 was reduced by 64%.

Adjusted ABR for all bleeds during the period between months 7 and 48 was reduced by 61%.

Primary endpoint demonstrating noninferiority of ABR during months 7 to 18 compared with lead-in period was met. Noninferiority comparison and mean ABR estimates were based on a repeated measures generalized estimating equations negative binomial regression model.

*In a noninferiority study, the ABR for all bleeds decreased from an average of 4.1 for prophylaxis during the lead-in period to 1.9 in months 7 to 18 post treatment, an ABR ratio of 0.46 (95% CI, 0.26-0.81).

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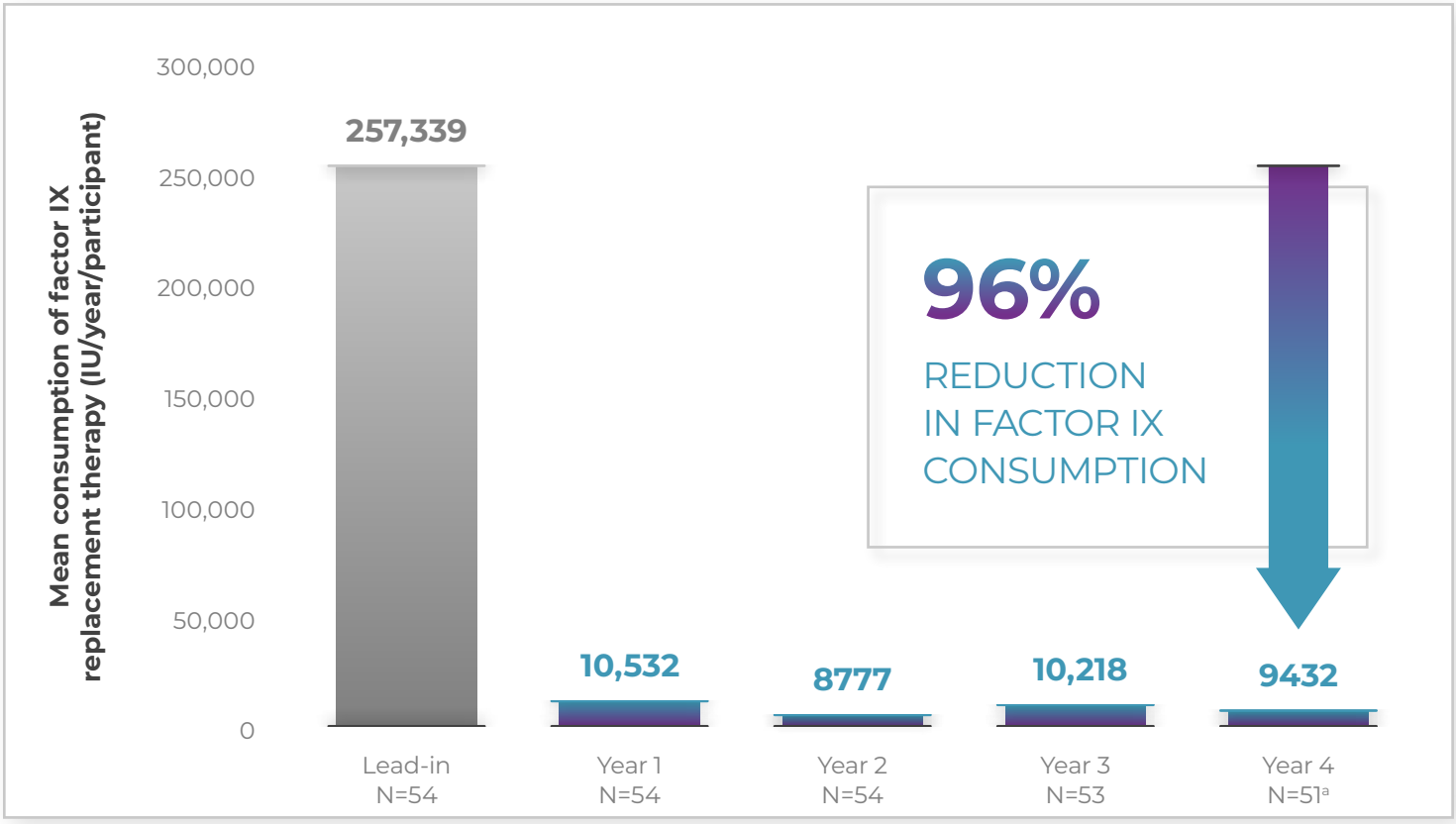
Annualized mean factor IX consumption decreased 96% from lead-in to 4 years post treatment[3]



Three patients required continuous prophylaxis after treatment*:

- **One non-responder patient** only received a partial dose (~10% of the dosage) due to an infusion reaction
- **Another non-responder patient** had a high preexisting NAb titer of 3212
- **One responder patient's** factor IX levels eventually declined to the 2% to 5% range; the patient's bleeding phenotype returned, and they resumed prophylaxis per protocol at month 30 post treatment

One additional patient required intermittent prophylaxis for approximately 20 weeks during months 7 to 18.

Abbreviations: AAV5, adeno-associated virus serotype 5; IU, international unit; NAb, neutralizing antibody.

[a]One patient died (prophylaxis free), 1 patient who remained on prophylaxis withdrew consent for efficacy assessment, and 1 patient had a liver transplant (prophylaxis free).

*A responder is defined as a participant who received the full dose of HEMGENIX, demonstrated factor IX expression, and discontinued continuous factor IX prophylaxis. Fifty-two subjects were included in the responder analysis set. The subject who discontinued the infusion of HEMGENIX after receiving approximately 10% of the full dose and the subject with the highest baseline AAV5 NAb titer of 1:3212 were excluded from the responder analysis set.

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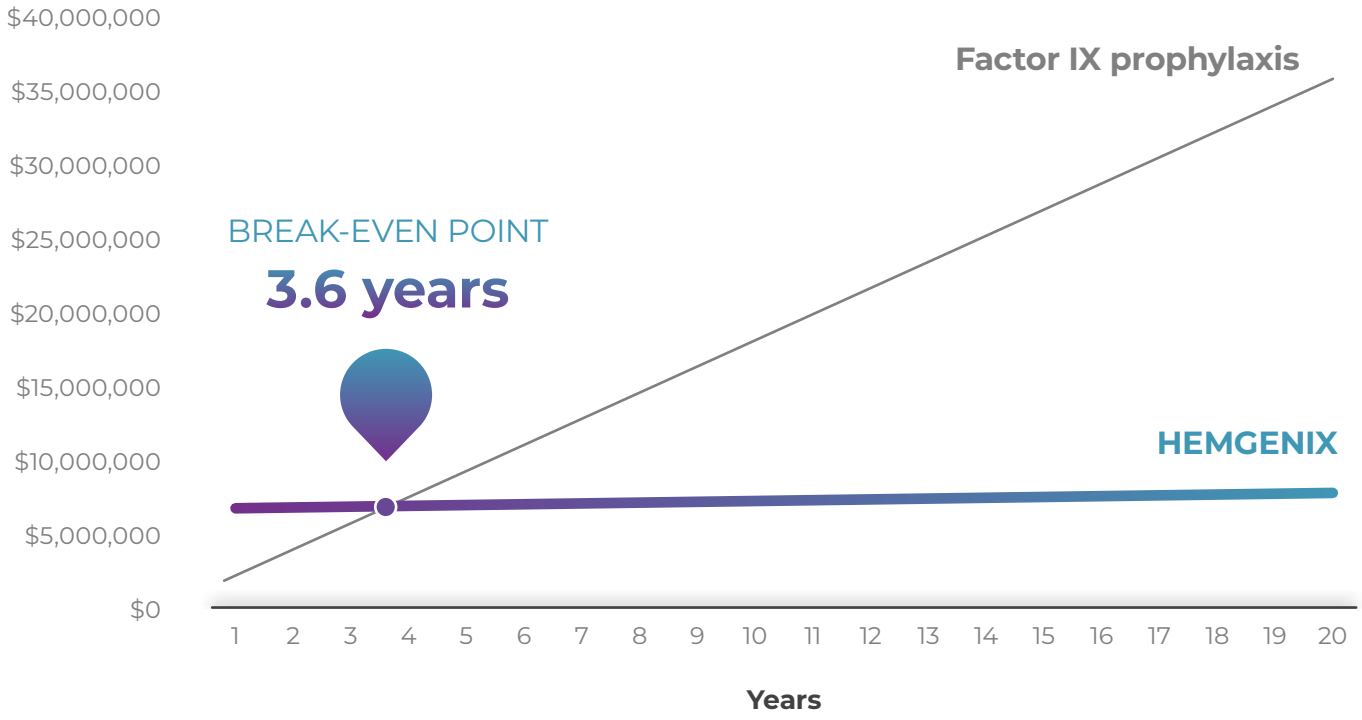
The average plan will see cost savings on HEMGENIX in fewer than 4 years[1,2]*

Modeled savings with HEMGENIX: gene therapy vs factor IX prophylaxis

Cumulative therapy costs, assuming 2 patients, the estimated number of qualified patients per million lives



In a study of hemophilia A patients with a mean duration of 6.3 years, 75% of commercially insured patients had the same commercial payer for the entire follow-up[4]

*Based on the HEMGENIX ADM. Accessed January 2025.

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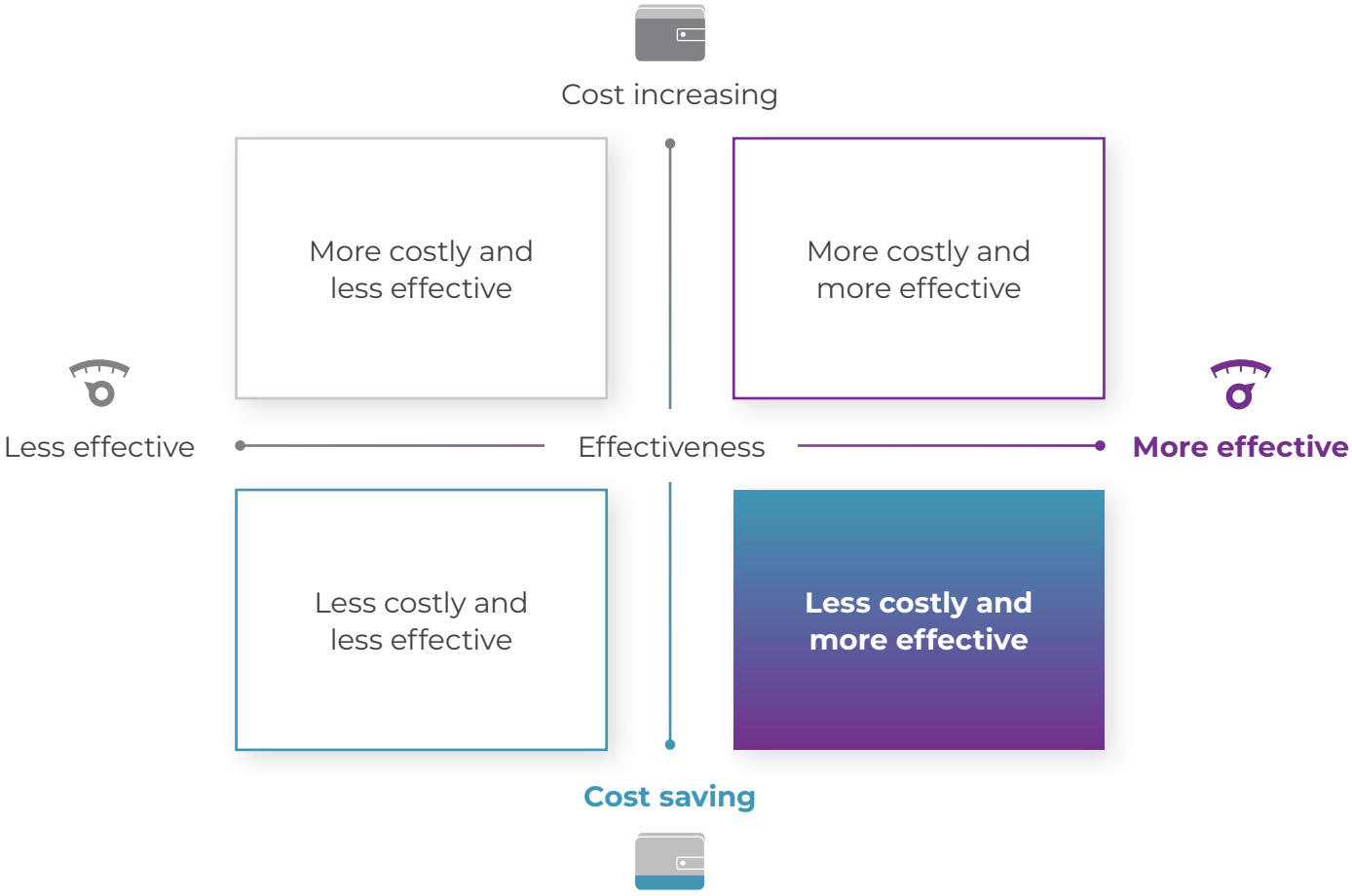
ICER determined that HEMGENIX will likely generate substantial cost savings and significant improvement in clinical outcomes[5]*

Cost-effectiveness framework[6]



The Institute for Clinical and Economic Review (ICER) conducted an analysis of the value of HEMGENIX for the treatment of hemophilia B.

In its analysis, ICER stated that HEMGENIX was projected to be a dominant treatment compared with factor IX, with lower costs and higher quality-adjusted life years[5]

Clinically, the evaluation concluded that there was high certainty of at least a small net benefit compared with factor IX prophylaxis

B+

ICER utilized a systematic literature review to assess the evidence on HEMGENIX compared with factor IX prophylaxis in adults eligible for factor prophylaxis for the treatment of hemophilia B.

*Compared with prophylactic factor IX use in adults eligible for factor prophylaxis for the treatment of hemophilia B.

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HEMGENIX value summary

Improved clinical outcomes and substantially reduced long-term costs with HEMGENIX*

37%

MEAN FACTOR IX ACTIVITY
was sustained at 4 years[3]

61%

REDUCTION IN ADJUSTED ABR
for all bleeds during months 7 to 48 post treatment remained significant[3†]

96%

DECREASE in annualized factor IX consumption[3‡]

3.6 years

The updated HEMGENIX ADM demonstrates that the average plan will see **cost savings in 3.6 years**[1,2§]

CSL Behring stands behind the promise of HEMGENIX with value-based agreements

*Relative to the current standard of care.
†ABR of all bleeds decreased from the average of 4.16 for prophylaxis during the lead-in period to 1.63 in months 7 to 48 after treatment. ABR was sustained at 4 years and satisfied the primary endpoint during months 7 to 18.
‡Mean factor IX consumption (IU/year/participant) decreased from 257,339 during the lead-in period to 9432 at year 4.[3]
§Based on the HEMGENIX ADM. Accessed January 2025.

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Important Safety Information

Warning and Precautions

Infusion Reactions

Infusion reactions, including hypersensitivity reactions and anaphylaxis, may occur. Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.

Hepatotoxicity/Hepatocellular Carcinoma

Post-dose, monitor for elevated transaminase levels. Consider corticosteroid treatment should elevations occur. The integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development. For patients with preexisting risk factors for hepatocellular carcinogenicity, perform regular (eg, annual) abdominal ultrasound and alpha-fetoprotein testing following administration.

Immune-mediated neutralization of the AAV5 vector capsid

Preexisting neutralizing anti-AAV antibodies may impede transgene expression at desired levels.

Monitoring Laboratory Tests

In addition to monitoring liver function, monitor for Factor IX activity and Factor IX inhibitors after administration.

Adverse Reactions

The most common adverse reactions (incidence ≥5%) were elevated ALT, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, nausea, malaise, and elevated AST.

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- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX is for single use intravenous infusion only.

Contraindications: None.

Please see full prescribing information for HEMGENIX.

To report SUSPECTED ADVERSE REACTIONS, contact the CSL Behring Pharmacovigilance Department at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. Data on file. Available from CSL Behring as DOF HGX-003. **2.** Data on file. Available from CSL Behring as DOF ETZ-001. **3.** Data on file. Available from CSL Behring as DOF HGX-010. **4.** He C, Hinds D, Pezalla E, et al. Health insurance coverage and switching among people with hemophilia A in the United States. *J Manag Care Spec Pharm.* 2022;28(2):232-243. doi:10.18553/jmcp.2021.21311 **5.** Tice JA, Walton S, Herce-Hagiwara B, et al; Institute for Clinical and Economic Review. *Gene Therapy for Hemophilia B and An Update on Gene Therapy for Hemophilia A: Effectiveness and Value.* Final evidence report. December 22, 2022. Accessed November 20, 2024. https://icer.org/wp-content/uploads/2022/12/ICER-Hemophilia-Policy-Recommendations-122222.pdf **6.** Cohen DJ, Reynolds MR. Interpreting the results of cost-effectiveness studies. *J Am Coll Cardiol.* 2008;52(25):2119-2126. doi:10.1016/j.jacc.2008.09.018

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