NOW WITH 5-YEAR DATA

# The value of HEMGENIX

## Exploring the value of a single-dose gene therapy vs the current standard of care

The healthcare economic information provided herein is pursuant to Section 114 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105-115) and Section 3037 of the 21st Century Cures Act (Public Law 114-255). It is intended for payers, formulary committees, or other similar entities with knowledge and expertise in the area of healthcare economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement.

## 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.

## Important Safety Information

### 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.

**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.**

**Please see Important Safety Information on page 8 and full prescribing information for HEMGENIX.**

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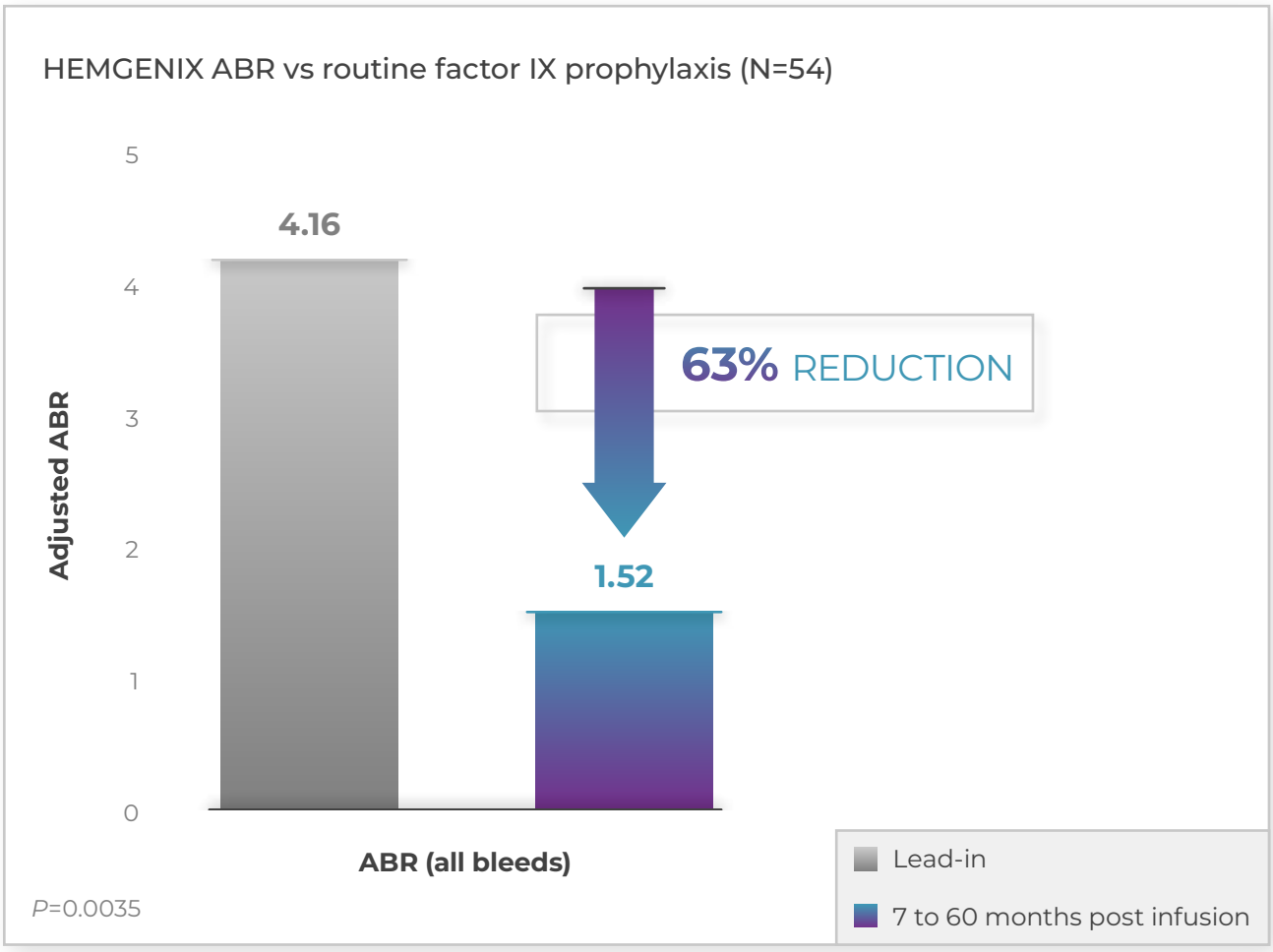
# At 5 years, patients treated with HEMGENIX showed sustained ABR reductions[1]

## A one-time infusion of HEMGENIX demonstrated noninferiority of annualized bleed rate (ABR) through 7 to 60 months compared with the lead-in period[1]




- Adjusted ABR for all bleeds during the period between months 7 and 18 was reduced by 64%[2]
- Adjusted ABR for all bleeds during the period between months 7 and 60 was reduced by 63%[1]

**85% reduction in annualized joint bleed rate compared with lead-in period (0.35 vs 2.34)[1]**

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.



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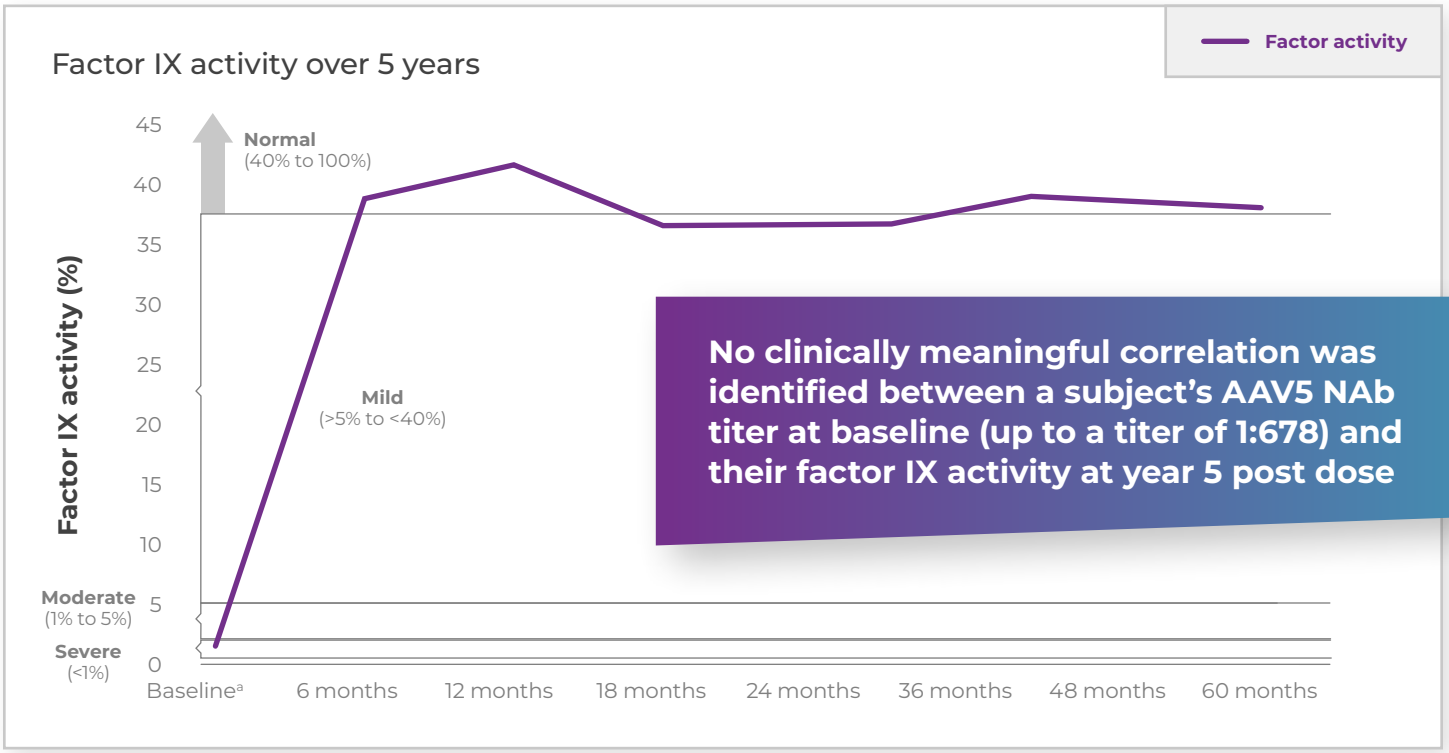
# Mean factor IX activity sustained at 36% at 5 years after single HEMGENIX infusion[1]




**No clinically meaningful correlation was identified between a subject's AAV5 NAb titer at baseline (up to a titer of 1:678) and their factor IX activity at year 5 post dose**

[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.

## Demonstrated reduction of factor IX utilization at 5 years

**Annualized mean factor IX consumption decreased**

**96%**

**from lead-in period to 5 years post treatment**

**94%**

**of patients (n=51/54)***

**eliminated routine factor IX prophylaxis and remained prophylaxis free** through 5 years post treatment

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

*Two patients experienced lack of efficacy. One patient had the highest NAb titer of 1:3212, and 1 patient received ~10% of the planned dose. One patient returned to factor IX prophylaxis at month 30 and their last factor IX activity levels were between the 2% and 5% range. An additional patient required intermittent prophylaxis for approximately 20 weeks during months 7 to 18.



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# Proven safety data through 5 years[1]

## At 5 years, the HEMGENIX safety profile remained favorable and consistent with previous observations, with no new treatment-related safety signals observed

| 0 | 0 | 0 | 2 |
|---|---|---|---|
| Treatment-related serious adverse events (AEs) | Factor IX inhibitors | Thrombotic events | Deaths, both unrelated to treatment |

Common treatment-related AEs (TRAEs) reported in >8% of patients (safety population)[1]

| TRAEs by MedDRA preferred term[a] | Up to year 5 | |
|---|---|---|
| | n (%) | Number of events |
| At least 1 TRAE[b] | 39 (72.2) | 100 |
| ALT increased | 10 (18.5) | 11 |
| Headache | 8 (14.8) | 9 |
| Influenza-like illness | 7 (13.0) | 8 |
| AST increased | 6 (11.1) | 7 |

**Three patients had infusion-related reactions that required a dose interruption[c]**

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; MedDRA, Medical Dictionary for Regulatory Activities.

[a]MedDRA Version 26.0 was used for coding.

[b]Includes possibly related or related.

[c]Infusion-related reactions were defined as any AEs related to the investigation of medical product administration procedures or unexpected reactions. Infusion reactions were any treatment-emergent AE occurring within 24 hours of infusion, qualifying for special notification, assessed as related or possibly related by the investigator, and considered as an infusion-related reaction during the safety assessment. They were infusion-site reaction, hypersensitivity (ie, urticaria), facial flushing, itching, headache, dizziness, etc.



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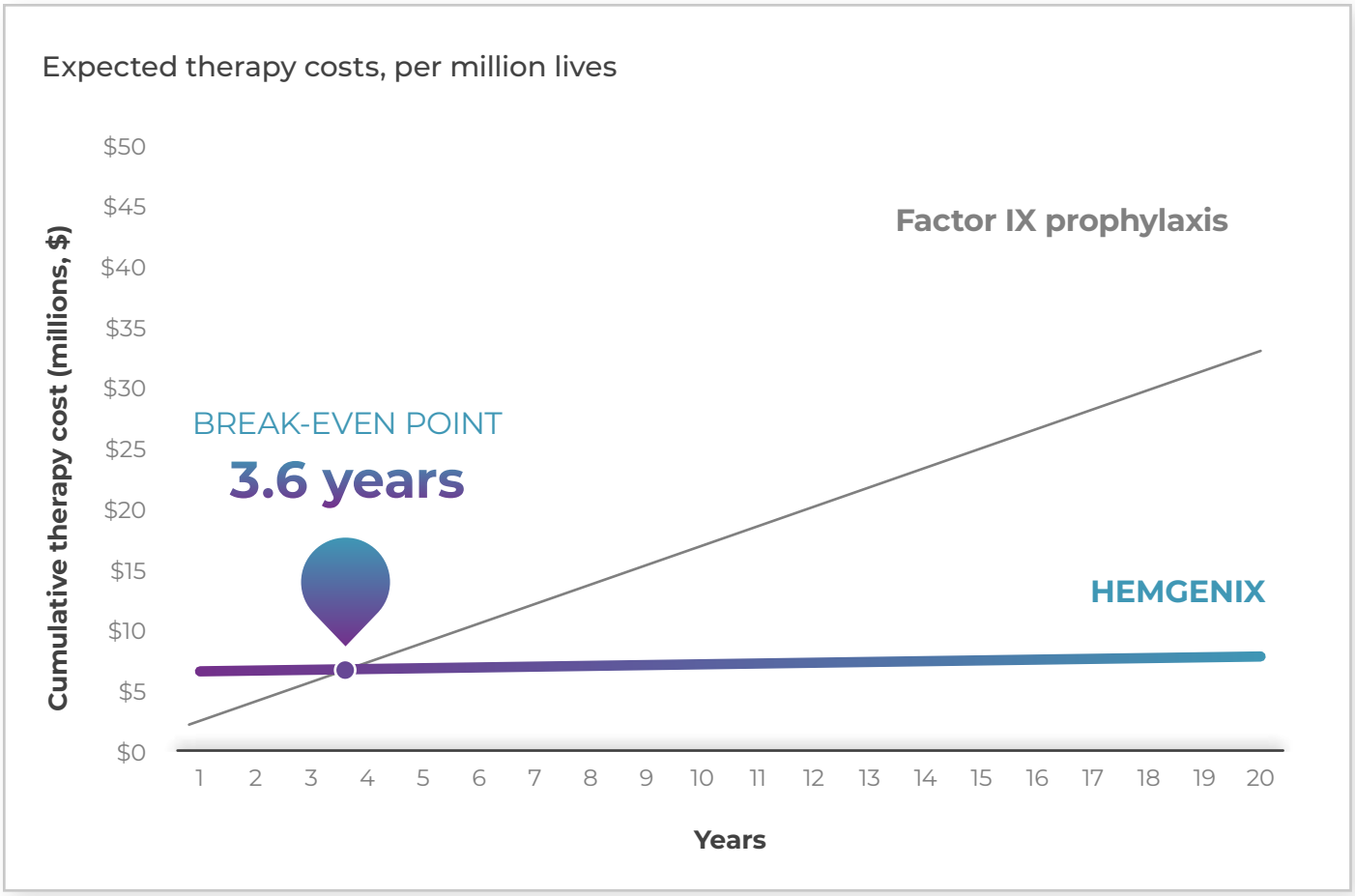
# HEMGENIX is estimated to start generating cost savings at 3.6 years[3]*

## Modeled savings with HEMGENIX: gene therapy vs factor IX prophylaxis†




**Payer retention among hemophilia B patients is strong—in a retroactive analysis of 666 patients, the average member stayed with their plan for 5.2 years[4]**

*Based on the HEMGENIX Access Decision Model. Accessed November 2025.
†Published wholesale acquisition cost (WAC) price.



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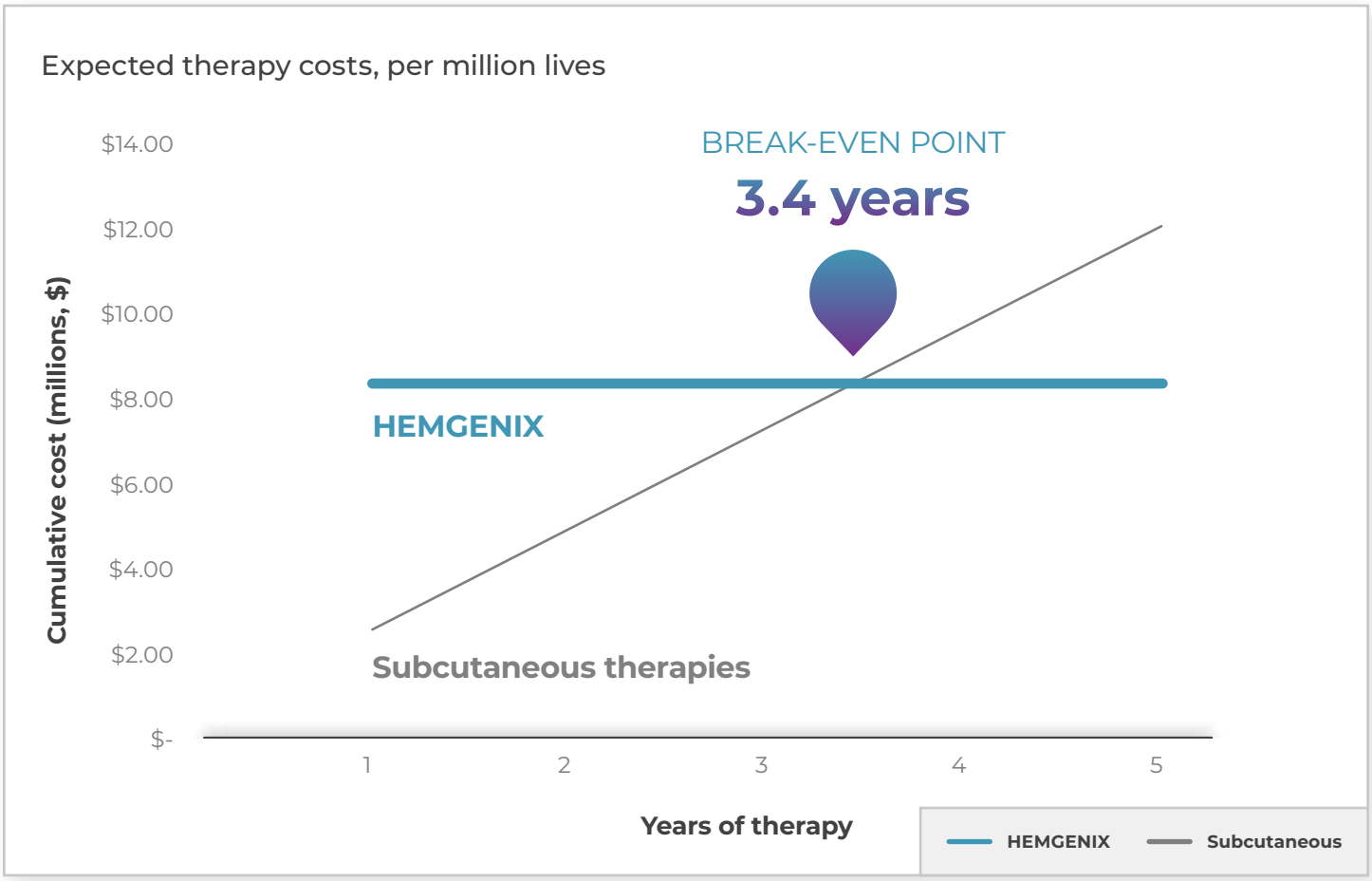
# HEMGENIX offers greater potential savings compared with subcutaneous options[5,6]*




**Using cost of drug therapy alone, plans could save $3.85 million over the course of 5 years if their indicated patients use HEMGENIX instead of subcutaneous therapies**

*Based on WAC, treatment regimen, and a 93.9 kg patient where appropriate.



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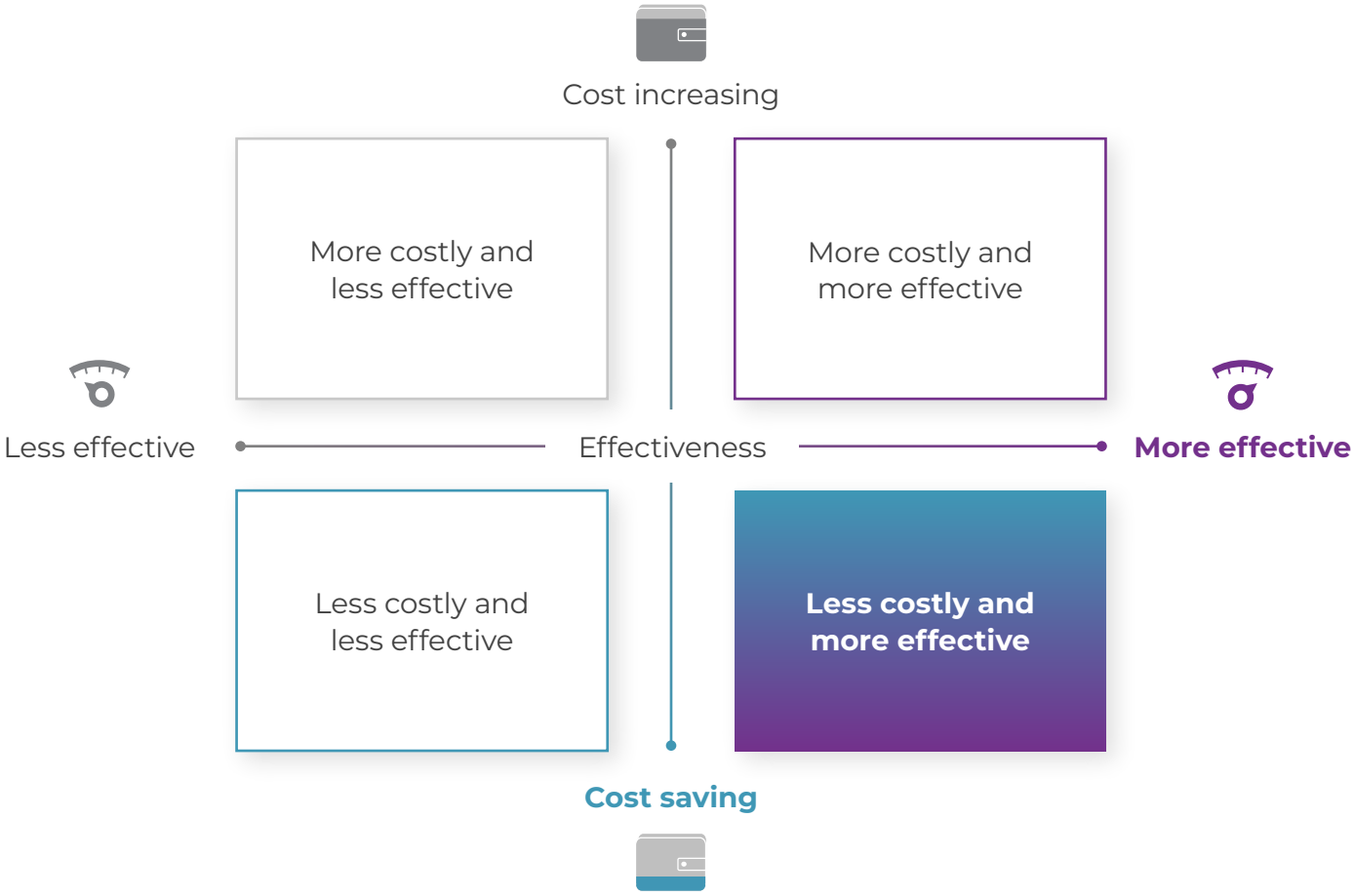
# In 2025, ICER reaffirmed their identification of HEMGENIX as a "high-value drug"[7]

## Cost-effectiveness framework[8]




In a previous analysis, the Institute for Clinical and Economic Review (ICER) appraised the value of HEMGENIX for the treatment of hemophilia B.[9]*

**ICER's base-case analysis projects net savings of over $6 million relative to the standard of care[9]**

**In its latest assessment, ICER calculates that redirecting first-year excess spending on drugs priced above their health benefit price benchmarks could fund treatment for 477 to 564 additional HEMGENIX patients[7]**

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



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# Important Safety Information and Indication

## 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.

## Indication

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## 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.** Pipe SW, Miesbach W, Recht M, et al; HOPE-B Study Group Investigators. Final analysis of a study of etranacogene dezaparvovec for hemophilia B. *N Engl J Med.* 2026;394(5):463-474. doi:10.1056/NEJMoa2514332 **2.** Pipe SW, Leebeek FWG, Recht M, et al. Gene therapy with etranacogene dezaparvovec for hemophilia B. *N Engl J Med.* 2023;388(8):706-718. doi:10.1056/NEJMoa2211644 **3.** Data on file. Available from CSL Behring as DOF HGX-003. **4.** Data on file. Available from CSL Behring as DOF HGX-012. **5.** Merative™ Micromedex® RED BOOK®. Accessed November 18, 2025. https://www.micromedexsolutions.com **6.** ClinicalTrials.gov. Accessed November 18, 2025. https://clinicaltrials.gov/ **7.** Agboola F, Lin GA, Lee W, et al; Institute for Clinical and Economic Review. *Launch Price and Access Report.* October 23, 2025. Accessed November 23, 2025. https://icer.org/wp-content/uploads/2025/10/ICER_2025_Launch-Price-and-Access-Final-Report_For-Publication.pdf **8.** 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 **9.** 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 23, 2025. https://icer.org/wp-content/uploads/2022/12/ICER-Hemophilia-Policy-Recommendations-122222.pdf



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