Long-term economic impact of etranacogene dezaparvovec versus extended half-life factor IX prophylaxis for severe or moderately severe hemophilia B in Spain

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INTRODUCTION

- Hemophilia B is a rare X-linked bleeding disorder caused by factor IX (FIX) deficiency. It affects around 300 people in Spain[1] and it is associated with a high clinical and economic burden, particularly in severe disease[2,3].
- Lifelong FIX prophylaxis is the current standard of care for the treatment of patients with severe hemophilia B in Spain[4,5].
- Etranacogene dezaparvovec (EDZ) is a gene therapy for severe and moderately severe hemophilia B patients which received reimbursement in Spain in September 2024[6,7]. In the HOPE-B trial, EDZ demonstrated sustained FIX expression, reduced bleeding rates, and near-complete elimination of exogenous FIX use over 5 years[8].
- Given the high upfront cost of EDZ, assessing long-term economic impact of EDZ versus extended half-life factor IX (EHL FIX) prophylaxis is essential to determine potential long-term savings for the Spanish healthcare system.

OBJECTIVE

- The aim of the present study was to evaluate the long-term economic impact of EDZ compared with EHL FIX prophylaxis in adult patients with severe or moderately severe hemophilia B in Spain.

METHODS

- A cost-offset model was developed to compare 2 hypothetical cohorts of 20 patients receiving either EDZ or EHL FIX prophylaxis over a 20-year time horizon. The population included in the analysis was consistent with HOPE-B patients[8] (adults previously treated with FIX prophylaxis) and assumed a mean body weight of 80 kg.
- EHL FIX cohort was represented as a weighted average of Alprolix® (35%), Idelvion® (55%), and Refixia® (10%), reflecting current treatment utilization in Spain[9].
- Clinical inputs included FIX activity and annual bleeding rates (ABR). Long-term maintenance of FIX activity levels ≥5 IU/dL following EDZ was estimated using a Bayesian projection model (**Table 1**)[10], based on the methodology previously described by Pan et al. (2026)[11].
- In the EDZ cohort, patients received a single infusion followed by 1 week of FIX prophylaxis therapy[6]. Patients remained free from prophylaxis while FIX activity was ≥5 IU/dL and returned to EHL FIX prophylaxis if FIX activity fell below that threshold over time. Patients treated with EHL FIX were assumed to maintain FIX activity levels ≥5 IU/dL throughout the analysis.
- ABR were derived from indirect treatment comparisons: EDZ ABR estimate (0.34) was based on an individual patient data comparison between 5-year HOPE-B study and Idelvion® pivotal trial, while EHL FIX estimate (2.34) was derived from the corresponding rate ratios versus EDZ and weighted average by each EHL FIX option utilization[12]. To avoid extrapolating bleeding benefits beyond the available evidence, EDZ ABR was applied only during the first 5 years; thereafter, EHL FIX ABR was conservatively assumed for both cohorts.

Table 1. Projected durability of response to EDZ[10]

Years since EDZ administration	%patients remaining free from FIX prophylaxis (≥5 IU/dL)	Years since EDZ administration	%patients remaining free from FIX prophylaxis (≥5 IU/dL)
Year 1	100.00%	Year 11	93.10%
Year 2	96.20%	Year 12	92.80%
Year 3	95.70%	Year 13	92.50%
Year 4	95.40%	Year 14	92.20%
Year 5	95.10%	Year 15	92.00%
Year 6	94.80%	Year 16	91.80%
Year 7	94.50%	Year 17	91.50%
Year 8	94.10%	Year 18	91.40%
Year 9	93.70%	Year 19	91.20%
Year 10	93.40%	Year 20	91.10%

- Only pharmacological costs (published ex-factory prices) were included[13]. In the EDZ cohort, costs captured the Spanish outcomes-based payment agreement (€2.688 million assumed to be six annual payments of €448,000 each, subject to maintenance of FIX activity ≥5 IU/dL)[14], plus 1 week of FIX prophylaxis therapy (€6,529). Non-responders to EDZ were assigned to EHL FIX prophylaxis costs. In the EHL FIX cohort, an annual prophylaxis cost of €339,502 per patient was considered. On-demand EHL FIX cost for breakthrough bleeds (€5,450 per episode) were applied to both cohorts (**Table 2**)[13,15-17].

Table 2. Costs of EHL FIX prophylaxis and on-demand EHL FIX for breakthrough bleeds[13,15-17]

EHL FIX	EHL FIX prophylaxis		On-demand EHL FIX	
	Regimen[a]	Mean annual cost/patient	Regimen[b]	Mean cost per bleed
Weighted average	–	**339,501.50 €**	–	**5,449.51 €**
Alprolix®	100 IU/kg q12d	300,906.67 €	46.07 IU/kg	4,570.14 €
Idelvion®	62.5 IU/kg q12d	348,833.33 €	30.00 IU/kg	5,520.00 €
Refixia®	40 IU/kg q7d	423,258.37 €	40.00 IU/kg	8,139.58 €

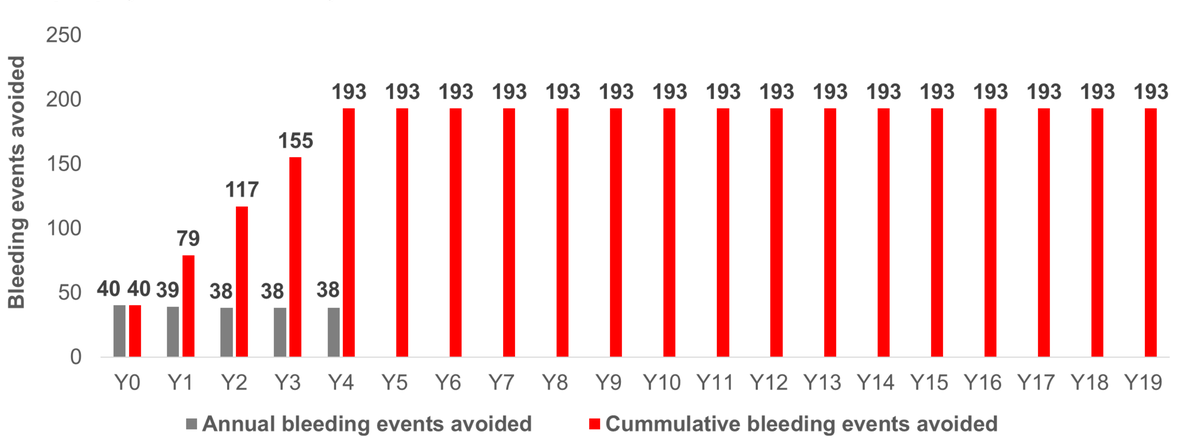
Dosing regimens were based on the SmPC and validated by clinical experts.
[a] Prophylaxis dosing assumptions: Alprolix® 100 IU/kg every 12 days (range: 10-14 days); Idelvion® 62.5 IU/kg (range: 50-75 IU/kg) every 12 days; Refixia® 40 IU/kg weekly.
[b] On-demand dosing assumptions: Idelvion® 30 IU/kg; Refixia® 40 IU/kg; Alprolix® 46.07 IU/kg.

- Annual and cumulative costs and breakthrough bleeding episodes were estimated over 20 years. Future costs were discounted at 3.0% annually according to Spanish pharmacoeconomic guidelines[18,19].

RESULTS

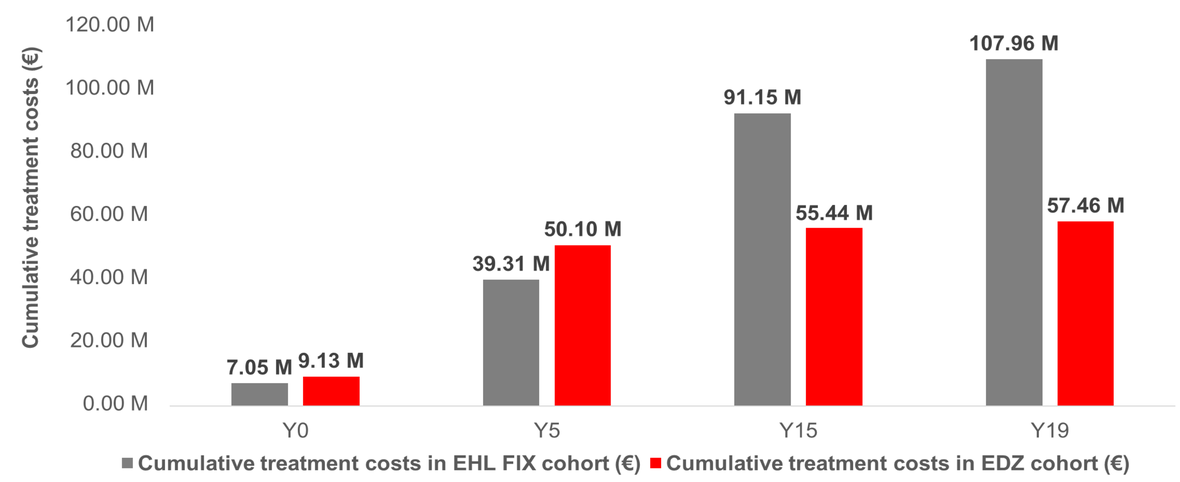
- ABR differences between both cohorts were conservatively assumed to apply only during the first 5 years of the analysis. As a result, after 20 years EDZ prevented 193 bleeding events versus EHL FIX prophylaxis, providing savings of €994,539 in avoided bleed-related treatment costs (**Figure 1**).

Figure 1. Annual and cumulative breakthrough bleeding events avoided with EDZ versus EHL FIX prophylaxis over a 20-year time horizon



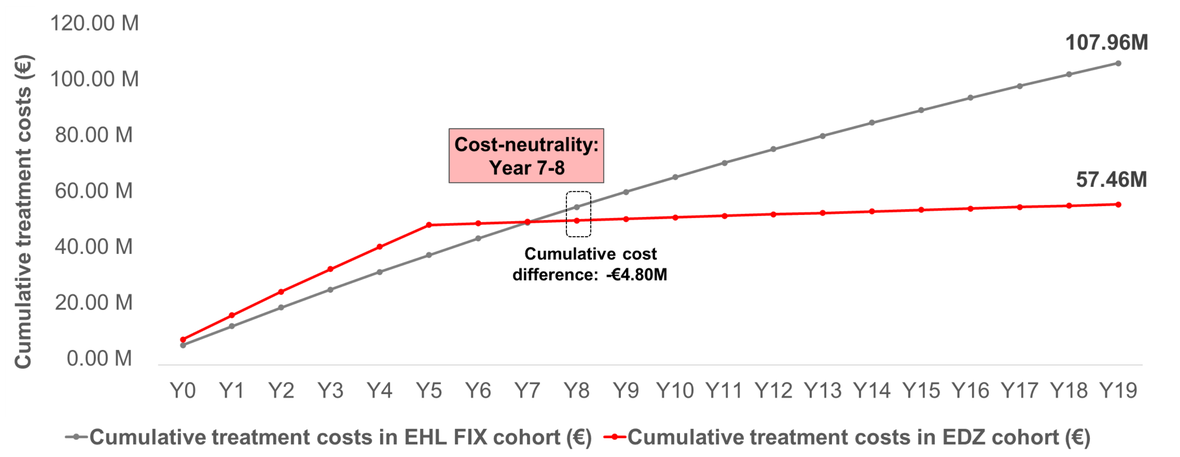
- Over 20 years, EDZ resulted in lower cumulative treatment costs versus EHL FIX prophylaxis, generating total savings of €50.51 million (€57.46 million vs €107.96 million) (**Figure 2**).

Figure 2. Cumulative total treatment cost for each cohort over a 20-year time horizon



- EDZ was associated with higher initial treatment cost; however, became cost-saving on an annual basis from year 6, reaching cumulative cost-neutrality between years 7 and 8 (**Figure 3**).

Figure 3. Evolution of cumulative total treatment cost for each cohort over a 20-year time horizon



- The projected cost savings were mainly attributable to the long-term durability of EDZ, with ~91% of treated patients expected to maintain FIX activity ≥5 IU/dL at year 20 and remaining free of continuous prophylaxis.

CONCLUSIONS

- **Assuming sustained long-term efficacy, EDZ could generate significant long-term savings versus EHL FIX prophylaxis by reducing continuous FIX utilization and lower bleed-related costs.**
- **These findings suggest that, even under conservative modelling assumptions to project long-term ABR, EDZ is expected to generate substantial long-term cost savings compared with EHL FIX prophylaxis for patients with severe or moderately severe hemophilia B in Spain.**

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Key: ABR - annualized bleeding rate; EDZ - etranacogene dezaparvovec; EHL - extended half-life; FIX - factor IX.

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