

Cost-Effectiveness of Fitusiran Prophylaxis Versus Factor VIII On-Demand or Prophylactic Therapy for Patients with Hemophilia A Without Inhibitors

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INTRODUCTION

Hemophilia: rare X-linked bleeding disorder (~850,000 globally; ~271,918 diagnosed), highlighting gaps in diagnosis and care.^{1,2}

Hemophilia A is most common (~17 per 100,000 males) caused by FVIII deficiency, leading to recurrent bleeding, joint damage, and disability.^{1,2}

Prevalence: ~33,000 affected in the US.³

Standard care: FVIII replacement (on-demand or prophylaxis), with prophylaxis recommended for severe disease.⁴

High burden: IV infusions, adherence issues, ~\$214k–\$870k/year.⁵

Fitusiran: is a subcutaneous siRNA therapy that reduces antithrombin; approved in 2025 with significant bleeding reduction in ATLAS trials.^{6,7}



STUDY AIM

To evaluate the **cost-effectiveness** of **fitusiran** prophylaxis compared with **FVIII prophylaxis** and on-demand FVIII therapy in patients with severe **hemophilia A** without inhibitors from a **US healthcare payer perspective**.



Model Design

State-transition, patient-level microsimulation

Population: males ≥12 years with severe hemophilia A (no inhibitors)

Lifetime horizon | 2-week cycle length

Health States

No bleed | Bleed | Joint bleed | Arthropathy | Joint replacement | Death



METHODS

Inputs

Efficacy: Fitusiran + comparators (ATLAS trials, literature)
Costs (2025 US\$): drug, administration, bleed-related care

Outcomes

Lifetime costs | QALYs | ICERs | Bleeds avoided

Analysis

Deterministic + probabilistic sensitivity analyses



CONCLUSION



- Fitusiran provided **higher QALYs at lower costs**, dominating FVIII prophylaxis and on-demand therapy.
- Reduced bleeding events and improved long-term outcomes.
- Results were **robust in sensitivity analyses**.
- Most sensitive to **annual dosing assumptions**.
- Supports fitusiran as a **high-value prophylactic strategy**.
- Highlights need for **real-world evidence** to optimize use and long-term outcomes.

RESULTS

Base-Case Analysis (US Healthcare Perspective)

Fitusiran was **least costly (~\$27M)** and **most effective (22.2 QALYs)** **Dominant strategy** vs. FVIII prophylaxis and on-demand therapy
Prevented:

- ❖ **554 bleeds** vs. on-demand FVIII
- ❖ **124 bleeds** vs. FVIII prophylaxis

Table 1: Costs & Effectiveness (Base-Case)

Strategy	Cost (US\$)	Incremental Cost	Eff. (QALYs)	Incremental Eff. (QALYs)	ICER
Fitusiran	26,951,467		22.184		
FVIII prophylaxis	37,916,688	10,965,221	21.881	-0.303	Abs. dominated
On-demand FVIII	38,714,044	11,762,577	15.031	-7.153	Abs. dominated

Sensitivity Analysis

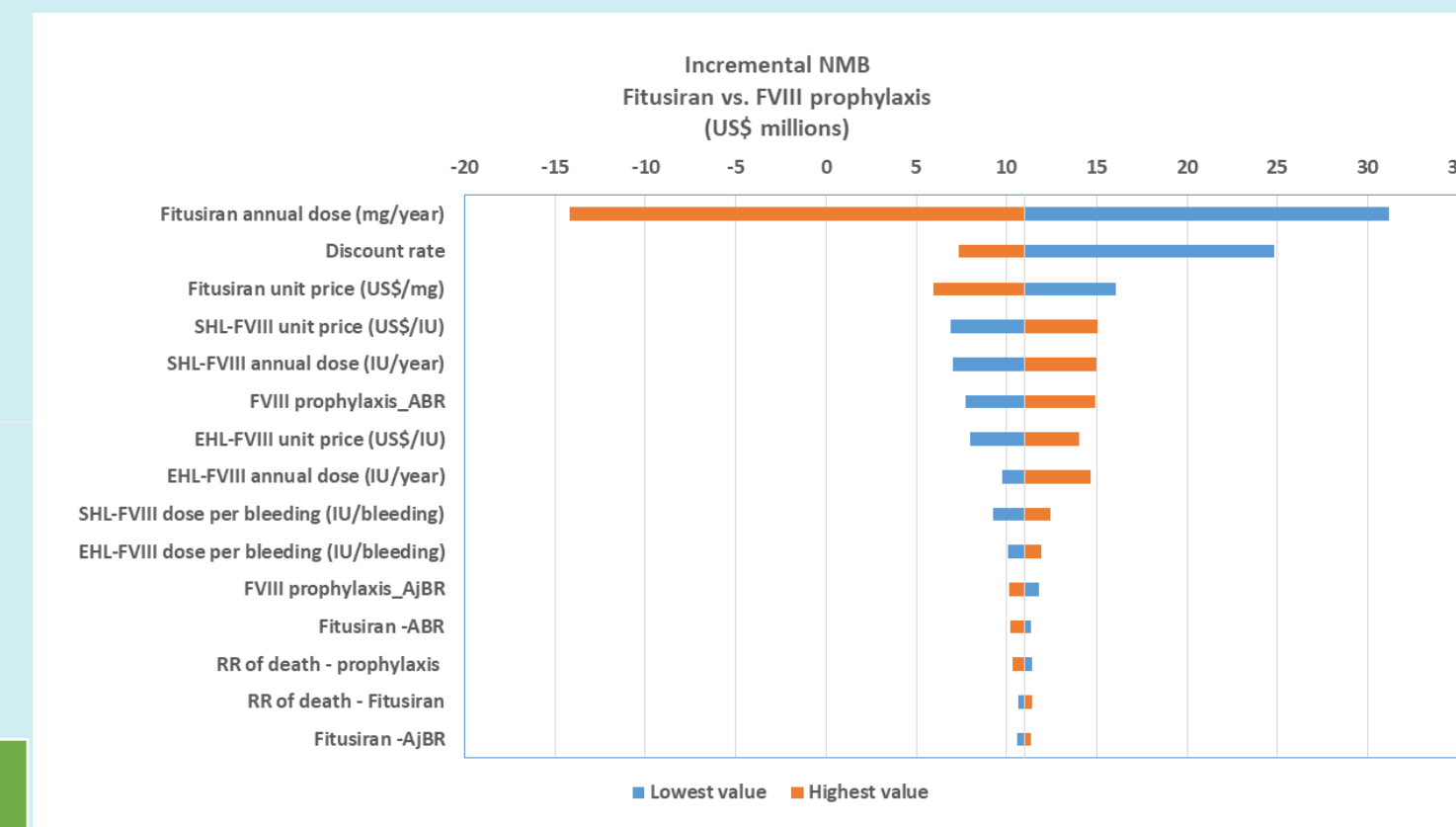


Figure 1: Tornado Diagram (INMB)

- Fitusiran remained **cost-effective across all parameters**
- Threshold loss of cost-effectiveness when annual dose exceeded:
 - ❑ **448 mg** (vs. on-demand FVIII)
 - ❑ **430 mg** (vs. FVIII prophylaxis)

Figure 2: Cost-Effectiveness Acceptability Curve (PSA)

- Preferred strategy in **>90% of simulations**
- Robust across WTP thresholds up to **\$200,000/QALY**

