EE706

Impact of Valoctocogene Roxaparvovec on the Economic Burden of Adults with Severe Hemophilia A Managed with Prophylaxis in the United States

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BACKGROUND

Hemophilia A is a rare X-linked hereditary bleeding disorder defined by a deficiency or absence of coagulation factor VIII (FVIII)[1]

- The extent of FVIII deficiency classifies the severity of the disease, with ~48% of people having severe disease[2]
- FVIII concentrate or hemostatic agents are used to prevent bleeding prophylactically, and acute breakthrough bleeds may be treated with additional FVIII replacement[1]
- ~83% of people with severe hemophilia A (PWHA) receive lifelong prophylaxis treatments[3]

Severe disease can be associated with significant disability and have a major impact on health-related quality of life[4,5]

Gene therapy has the potential to replace the high annual cost of prophylaxis with a single upfront treatment cost and may also affect non-medical costs in multiple years, significantly altering the societal costs of severe hemophilia A in the future

OBJECTIVE

To estimate the reduction in societal economic burden among patients with severe hemophilia A without inhibitors currently managed with prophylaxis in the US after the introduction of valoctocogene roxaparvovec

METHODS

An economic model was developed to estimate the change in burden of a cohort of adult males with severe hemophilia A managed with prophylaxis after the introduction of valoctocogene roxaparvovec over a 10-year horizon

METHODS CONTINUED

The number of adult males with severe hemophilia A without inhibitors currently managed with prophylaxis was calculated using CDC Community Count estimates of hemophilia A prevalence and severity, national estimates for US Census age and sex distribution among males, and literature-based inputs[2,3,6,7] (**Figure 1**)

Prior to gene therapy availability, the analysis assumed treatment of hemophilia A was split equally between FVIII prophylaxis and emicizumab use

Direct medical costs (FVIII concentrate or emicizumab, other non-FVIII medical costs) and non-medical costs (early retirement, caregiver, underemployment, absenteeism, transfer payments) were considered (**Table 1**)

- The price of valoctocogene roxaparvovec was assumed to be $2.9M per average weight person, 10% of PWHA were assumed to be treated with valoctocogene roxaparvovec, and 4% of PWHA treated with valoctocogene roxaparvovec were assumed to return to prophylaxis annually
- Direct medical cost inputs were sourced from nationally representative administrative claims databases[8,9]
- Non-medical cost inputs were derived from the cross-sectional, patient-reported survey, Cost of Severe Hemophilia across the US: a Socioeconomic Survey (CHESS US+), as well as the Patient Reported Outcomes Burdens and Experiences (PROBE) multinational survey[10,11]

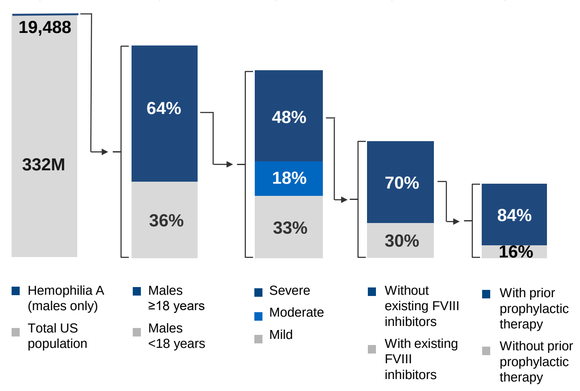
The analysis reported annual economic burden in aggregate and distributed among different payers (public insurer [Medicare/Medicaid], employer/private insurer, and household). The analysis also accounted for transfer payments, which allocated the economic burden among the considered payers

All costs are reported in 2022 USD

MODEL INPUTS

Figure 1

Adult Males with Severe Hemophilia A without Inhibitors Managed with Prophylaxis in the US



[a] CDC Community Count (March 2022 data cut) was used to calculate the proportion of males in the 2 age categories and projected 2021 US Census data (from 2020 Census) were used to split the 11-19 age group into an 11-17 age group and an 18-19 age group.

[b] Disease severity distribution by age groups is reported by CDC Community Count (March 2022 data cut). Projected 2021 US Census data were used to calculate proportion of males ≥18 years in the disease severity distribution. The proportion of males with severe disease was calculated as the number of males ≥18 years with known severe disease divided by the total number of males ≥18 years with hemophilia A. In particular, this calculation assumes that none of the males with unknown disease severity have severe disease.

[c] This value is sourced from a severe hemophilia A population, age and gender not specified.

[d] This value is sourced from a severe hemophilia A population treated at HTCs and could be a slight over-estimation of prior prophylaxis use in a general adult hemophilia A population.

Table 1

Severe Hemophilia A Costs, Per Person Per Year

Direct Medical Costs (2022 USD)	Per Person Per Year
Valoctocogene roxaparvovec	$2,900,000 (one-time cost)
Gene therapy treatment-related costs[a,b]	$55,316 (first year only cost)
FVIII concentrate[8,a]	$695,311
Emicizumab[9,a,c]	$758,425
Other medical costs[8,a,d]	$22,098

Non-Medical Costs (2022 USD)[a]	Per Person Per Year, Without Gene Therapy[10]	Per Person Per Year, With Gene Therapy[10,11]
Early retirement	$7,550	$7,550
Caregiver	$3,801	$3,801
Underemployment	$2,431	$2,431
Absenteeism	$1,071	$300
Other non-medical costs[e]	$904	$904

[a] Costs were inflated to 2022 USD.

[b] PWHA receiving gene therapy are assumed to incur specific treatment-related costs in the first year, including an initial 4 weeks of FVIII prophylaxis, corticosteroid use, hepatic panels, and other tests.

[c] Includes additional FVIII use.

[d] Includes all non-FVIII-related medical and pharmacy costs.

[e] Includes transportation to HTC visits, over-the-counter medication, alternative and complementary therapies, and device and home alteration costs.

RESULTS

There are an estimated 3,480 US adults with severe hemophilia A without inhibitors managed with FVIII or emicizumab prophylaxis (**Figure 1**)

PWHA were most commonly insured by private health plans (55%), Medicaid (31%), Medicare (11%), and dual Medicare/Medicaid (3%)[12]

Without the availability of gene therapy, the national economic burden of severe hemophilia A among adults without inhibitors is estimated to be $2.5 billion annually, of which $1.4 billion is borne by employers/private insurers, $1.0 billion is borne by the public, and $50 million is borne by households (**Table 2**)

- Nationally, direct medical costs account for over 97% of total costs and are the main driver of economic burden
- For each household, non-medical costs are the main driver of economic burden among households of PWHA, accounting for over 78% of total costs (economic burden per household is $14,334 annually)

Assuming 10% (348 adults) of the modelled cohort receive valoctocogene roxaparvovec in year 1, the cumulative 10-year reduction in national economic burden is $564 million (**Figure 2/Table 3**)

- After 4 years, the introduction of valoctocogene roxaparvovec will result in cost savings
- The 10-year economic reductions for the public payer, employer/private insurance, and households are estimated to be $230 million, $334 million, and $422,000, respectively
- Nationally, over 99% of the reduction in economic burden is attributable to a change in direct medical costs

Among PWHA treated with valoctocogene roxaparvovec, the introduction of valoctocogene roxaparvovec will result in a 30% reduction in total economic burden over 10 years, from $5.5 million/PWHA managed with prophylaxis to $3.9 million/PWHA treated with valoctocogene roxaparvovec

- There is a 14-17% reduction in household-borne non-medical costs among PWHA treated with valoctocogene roxaparvovec over 10 years, driven by decreased absenteeism after the availability of valoctocogene roxaparvovec (**Figure 3**)

Assuming 4% of patients treated with valoctocogene roxaparvovec resume prophylaxis annually,[13] post-gene therapy prophylaxis is estimated to cost $513 million over 10 years

Table 2

Current Annual Economic Burden of Severe Hemophilia A, by Payer

	Public (Medicare, Medicaid, Other Government)	Employer/ Private	Household	Total, All Payers[a]
Direct medical costs	$991.8 M	$1,430.1 M	$10.8 M	$2,432.7 M
Non-medical costs	$9.7 M	$6.0 M	$39.1 M	$54.8 M
Total, by payer[a]	**$1,001.5 M**	**$1,436.1 M**	**$49.9 M**	**$2,487.5 M**
Total, per PWHA	**--**	**--**	**$14,334**	**--**

M, millions.
[a] Due to rounding, some totals may not correspond with the sum of the individual components.

Table 3

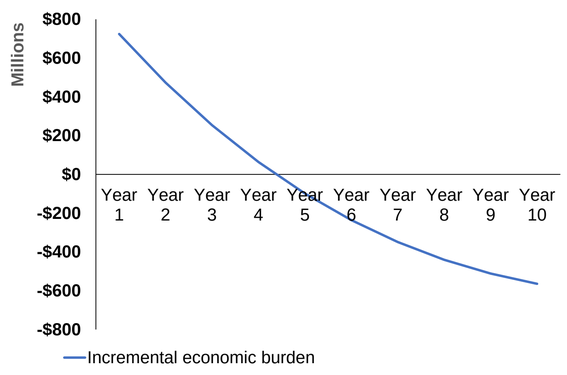
Cumulative Economic Burden of Severe Hemophilia A[a]

	Year 1	Year 3	Year 5	Year 10
Without gene therapy available				
	$2,487.5 M	$7,034.1 M	$11,050.5 M	$19,064.5 M
With gene therapy available				
	$3,211.0 M	$7,287.5 M	$10,951.6 M	$18,500.3 M
Incremental difference				
	$723.5 M	$253.4 M	-$98.9 M	-$564.2 M

M, millions.
[a] Assumes 10% uptake of valoctocogene roxaparvovec and 4% of PWHA treated with valoctocogene roxaparvovec were assumed to return to prophylaxis annually.

Figure 2

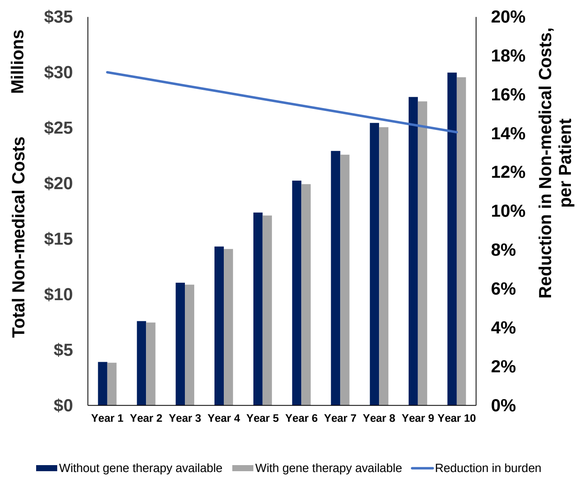
Incremental Cumulative Economic Burden of Severe Hemophilia A[a]



[a] Assumes 10% uptake of valoctocogene roxaparvovec and 4% of PWHA treated with valoctocogene roxaparvovec were assumed to return to prophylaxis annually.

Figure 3

Cumulative Household Non-medical Costs and Associated Reductions from Gene Therapy Introduction[a]



[a] Assumes 10% uptake of valoctocogene roxaparvovec and 4% of PWHA treated with valoctocogene roxaparvovec were assumed to return to prophylaxis annually.

LIMITATIONS

Medical cost inputs were derived from administrative claims databases and reflect commercial beneficiaries. The model used an assumed payment scaling factor to estimate costs for other payers

Non-medical cost inputs were derived from patient-reported survey data and therefore may be subject to selection bias, recalls bias, and/or potential errors in data abstraction

Insurance out-of-pocket maximums, availability of paid sick leave, and availability of public or private disability insurance were considered when allocating economic burden among payers. However, some payment amounts were assumption-based

The national economic burden may be underestimated as there may be costs associated with severe hemophilia A not considered in the analysis. Additionally, this analysis reflects the treatment landscape prior to the availability of antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl for prophylaxis treatment

The rate of returning to prophylaxis is a key model input and estimates incorporate simplifying assumptions based on clinical trial data. Estimates may not capture the variability in return to prophylaxis on an annual and per-patient basis that will likely be seen in the real world

- Over the entire follow-up period in the GENEr8-1 clinical trial, 17 out of 134 patients returned to prophylaxis use with FVIII products or other hemostatic agents;[13] these data were used to model an approximate return to prophylaxis rate of ~4% per year

Potential outcomes-based agreements for gene therapy treatment were not considered in the overall estimates of economic burden in this analysis

CONCLUSIONS

Although a rare disease, severe hemophilia A is associated with significant economic burden on healthcare payers, households of PWHA, and society

While the initial, one-time cost of valoctocogene roxaparvovec is significant, its use will reduce the overall societal economic burden of severe hemophilia A and result in cost-savings after 4 years

This study highlights that reductions in economic burden for households of PWHA are primarily driven by decreases in absenteeism after treatment with gene therapy

Understanding the significant societal burden of hemophilia among PWHA, caregivers, and families should be considered as part of technology or value assessments when considering treatment alternatives to the current standard of care

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DISCLOSURES

This study was funded by BioMarin Pharmaceutical, Inc, which developed valoctocogene roxaparvovec to treat severe hemophilia A.

TW, CR, KC, and NK are employees of Analysis Group, a consulting company that was contracted by BioMarin Pharmaceutical to conduct this analysis and develop this poster. EC and SS are employees and shareholders of BioMarin. EP and MS received consulting fees from BioMarin.