Impact of Gene Therapy 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 marked by a deficiency or absence of coagulation factor VIII (FVIII)[1]

- The extent of FVIII deficiency defines the severity of the disease, with ~48% of people with severe disease[2]
- Prophylaxis with FVIII concentrate or hemostatic agent is used to prevent bleeding, and acute bleeds are treated with additional FVIII replacement[1]
- ~83% of people with severe hemophilia A (PWHA) are on 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 quantify the expected reduction in societal economic burden of severe hemophilia A without inhibitors currently managed with prophylaxis in the US after the anticipated approval of valoctocogene roxaparvovec

METHODS

An economic analysis was performed to estimate the expected reduction in societal economic burden among one cohort of adult males with severe hemophilia A without inhibitors managed with prophylaxis over a 10-year model horizon

- The number of eligible adult males with severe hemophilia A without inhibitors managed with prophylaxis was calculated using CDC 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**)

The analysis assumed half of the population was managed with FVIII prophylaxis and the other half with emicizumab prior to gene therapy availability

The analysis considered direct medical costs (e.g., FVIII concentrate or emicizumab, other medical costs) and non-medical costs (e.g., early retirement, caregiver, underemployment, absenteeism, other non-medical costs) (**Table 1**)

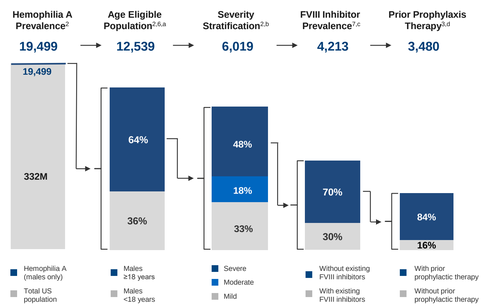
- The price of valoctocogene roxaparvovec was assumed to be $2.5M per average weight person, 10% of PWHA were assumed to be newly treated with valoctocogene roxaparvovec, and 1.5% to 2.5% of PWHA treated with valoctocogene roxaparvovec were assumed to return to prophylaxis each year
- Direct medical cost inputs were sourced from nationally representative administrative claims databases[8,9]
- Non-medical cost inputs were sourced from cross-sectional, patient-reported survey data, Cost of Severe Hemophilia across the US: a Socioeconomic Survey (CHESS US+)[10]

The analysis reported total annual economic burden and annual economic burden distributed among different payers (public insurer [Medicare/Medicaid], employer/private insurer, and household) and accounted for transfer payments when allocating 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	Per Person Per Year (2022 USD)
Valoctocogene roxaparvovec	$2,500,000 (one-time cost)
Gene therapy treatment-related costs[a]	$55,316 (first year only cost)
FVIII concentrate[8]	$695,311
Emicizumab[9,b]	$758,425
Other medical costs[8,c]	$22,098
Non-Medical Costs[10]	**Per Person Per Year (2022 USD)**
Early retirement	$7,550
Caregiver	$3,801
Underemployment	$2,431
Absenteeism	$1,071
Other non-medical costs[d]	$904

[a] 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.
[b] Includes additional FVIII use.
[c] Includes all non-FVIII-related medical and pharmacy costs.
[d] 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/Medicare (3%)

The national economic burden was projected 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**)

- The per household economic burden is $14,334 annually
- Nationally, direct medical costs are the main driver of economic burden, accounting for over 97% of total costs
- However, non-medical costs are the main driver of economic burden in households, accounting for over 78% of total costs borne by households

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.

Assuming 10% (348 adults) of the modelled cohort receive valoctocogene roxaparvovec in year 1, the cumulative 10-year reduction in national economic burden ranges from $854 to $982 million, depending on the rate at which treated PWHA return to prophylaxis after receiving gene therapy (**Table 3**)

- The 10-year economic reductions for the public payer, employer/private insurance, and households range from $349 to $401 million, $505 to $581 million, and $192,000 to $201,000, respectively

Among the modelled cohort, this represents a 4% to 5% reduction in total economic burden over 10 years; among PWHA treated with valoctocogene roxaparvovec, this represents a 45% to 52% reduction in total economic burden over 10 years, depending on return to prophylaxis assumptions (**Table 4**)

- Nationally, over 99% of the reduction in economic burden is attributable to a change in direct medical costs

After 4 years, the introduction of valoctocogene roxaparvovec will result in cost savings

RESULTS

Table 3 Incremental Economic Burden of Severe Hemophilia A, by Payer and Return to Prophylaxis Assumption[a]

	Year 1	Year 3	Year 5	Year 10
Return to prophylaxis assumption of 1.5% annually				
Public	$242.6 M	$49.5 M	-$112.2 M	-$401.1 M
Employer/ Private	$351.2 M	$71.6 M	-$162.4 M	-$580.6 M
Household	-$28,175	-$78,478	-$121,411	-$201,363
Total[b]	$593.8 M	$121.0 M	-$274.7 M	-$981.9 M
Return to prophylaxis assumption of 2% annually				
Public	$242.6 M	$50.3 M	-$107.2 M	-$374.9 M
Employer/ Private	$351.2 M	$72.9 M	-$155.2 M	-$542.8 M
Household	-$28,175	-$78,080	-$120,160	-$196,505
Total[b]	$593.8 M	$123.1 M	-$262.5 M	-$918.0 M
Return to prophylaxis assumption of 2.5% annually				
Public	$242.6 M	$51.2 M	-$102.2 M	-$348.8 M
Employer/ Private	$351.2 M	$74.1 M	-$147.9 M	-$505.0 M
Household	-$28,175	-$77,681	-$118,908	-$191,646
Total[b]	$593.8 M	$125.2 M	-$250.2 M	-$854.1 M

M, millions.
[a] Assumes 10% uptake of valoctocogene roxaparvovec.
[b] Due to rounding, some totals may not correspond with the sum of the individual components.

Table 4 Percent Reduction in Economic Burden

Return to Prophylaxis Assumption	1.5%	2%	2.5%
Percent reduction among modelled cohort by year 10	5%	5%	4%
Percent reduction per PWHA treated with valoctocogene roxaparvovec by year 10	52%	48%	45%

LIMITATIONS

Medical cost inputs were sourced from administrative claims databases and reflect commercial beneficiaries; a payment scaling factor was assumed for other payers

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

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

There may be other costs associated with severe hemophilia A not considered in the analysis; national economic burden may be underestimated

Estimates of return of prophylaxis, a key model input, incorporate simplifying assumptions based on clinical trial data and does not capture the variability in return to prophylaxis on an annual basis that will likely be seen in the real world

- At a mean follow-up duration of 122.3 weeks, 6 out of 132 patients returned to prophylaxis in the GENEr8-1 trial[11]

Potential outcomes-based agreements for gene therapy were not considered in the analysis

CONCLUSIONS

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

The introduction of valoctocogene roxaparvovec is expected to significantly reduce the economic burden associated with the treatment of hemophilia A over 10 years

The study highlights that the main reduction in burden is primarily associated with change in direct medical costs and after 4 years, gene therapy treatment will result in cost saving

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

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DISCLOSURES

This study was funded by BioMarin Pharmaceutical, Inc, which is currently developing 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 is an employee and shareholder of BioMarin. EP received consulting fees from BioMarin. MS received consulting fees from BioMarin.