VALUE IN HEALTH ▮ (2016) ▮▮▮–▮▮▮

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Budget Impact Analysis of Prolonged Half-Life Recombinant FVIII Therapy for Hemophilia in the United States

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ABSTRACT

Background: Hemophilia A is a factor VIII deficiency, associated with spontaneous, recurrent bleeding episodes. This may lead to comorbidities such as arthropathy and joint replacement, which contribute to morbidity and increased health care expenditure. Recombinant factor VIII Fc fusion protein (rFVIIIFc), a prolonged half-life factor therapy, requires fewer infusions, resulting in reduced treatment burden. **Objective:** Use a budget impact analysis to assess the potential economic impact of introducing rFVIIIFc to a formulary from the perspective of a private payer in the United States. **Methods:** The budget impact model was developed to estimate the potential economic impact of adding rFVIIIFc to a private payer formulary across a 2-year time period. The eligible patient population consisted of inhibitor-free adults with severe hemophilia A, receiving recombinant-based episodic or prophylaxis treatment regimens. Patients were assumed to switch from conventional recombinant factor treatment to rFVIIIFc. Only medication costs were included in the model. **Results:** The introduction of rFVIIIFc is estimated to have a budget impact of 1.4% ($0.12 per member per month) across 2 years for a private payer population of 1,000,000 (estimated 19.7 individuals receiving treatment for hemophilia A). The introduction of rFVIIIFc is estimated to prevent 124 bleeds across 2 years at a cost of $1891 per bleed avoided. **Conclusions:** Hemophilia A is a rare disease with a low prevalence; therefore, the overall cost to society of introducing rFVIIIFc is small. Considerations for comprehensively assessing the budget impact of introducing rFVIIIFc should include episodic and prophylaxis regimens, bleed avoidance, and annual factor consumption required under alternative scenarios.

Keywords: budget impact, economic impact, hemophilia A, rFVIIIFc.

Introduction

Hemophilia A is an inherited, lifelong bleeding disorder characterized by prolonged or spontaneous bleeding due to the lack of clotting factor VIII (FVIII) in the body. Severe hemophilia A can cause spontaneous or traumatic bleeding into the joints, soft tissues, muscles, and body cavities, often leading to chronic arthropathy. Arthropathy is associated with irreversible joint damage, severe joint pain, and functional impairment in later life. Treatment for hemophilia involves FVIII replacement therapy to control bleeding, which can be given as episodic or prophylactic treatment. Episodic treatment is used to treat an acute bleeding event [1–3]. *Prophylactic treatment*, defined as regular infusions of factor therapy taken to prevent bleeding events rather than treating events as they occur, is recommended as the optimal therapy for individuals with severe hemophilia A according to the Medical and Scientific Advisory Council [4]. Although the same medications are used in both settings, prophylaxis is associated with higher direct drug costs than episodic treatment; nevertheless, in addition to clinical benefits of preventing bleeding episodes and subsequent joint damage [5], patients on prophylactic treatment generally exhibit higher quality-of-life scores than do those treated episodically [6]. In addition, prophylaxis reduces hospital/emergency room visits and indirect costs associated with patients with hemophilia [5,7,8].

Historically, treatment with conventional prophylaxis regimens for hemophilia A requires infusion treatment 3 to 4 times per week. Such frequent dosing places a high treatment burden on patients and caregivers. Recombinant FVIII Fc (rFVIIIFc) is a first-in-class prolonged half-life factor therapy that was developed to prolong the half-life of FVIII and allow for fewer infusions compared with products approved at present. The prophylaxis dosing approved by the US Food and Drug Administration for rFVIIIFc is an individualized regimen of 50 IU/kg every 4 days (i.e., 1–2 times per week) with patient-specific adjustments ranging from 25 to 65 IU/kg every 3 to 5 days [9]. In the phase 3 extension trial of rFVIIIFc (Long-Term Safety and Efficacy of rFVIIIFc in the

Conflict of interest: B. Buckley, E. Hall II, and J. Kendter are employees of and shareholders in Biogen.

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1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2016.09.2396

Prevention and Treatment of Bleeding Episodes in Previously Treated Participants With Hemophilia A [ASPIRE trial]), patients on an individualized regimen and a once-weekly prophylaxis regimen (65 IU/kg every 7 days) had reported median annualized bleeding rates (ABRs) of 0.66 and 2.03 bleeding episodes per patient, respectively [10,11], demonstrating that doses as low as once per week are still effective at preventing bleeds but with fewer doses and reduced overall factor consumption than conventional prophylaxis therapy [12,13]. Fewer doses result in less vein access and less time required for disease management, which may lead to better adherence and quality of life for both patients and caregivers [14]. Across all arms in the phase 3 trial, 87.3% of bleeding episodes were resolved with one infusion and 97.8% were controlled with one or two infusions, establishing the benefit of the prolonged half-life therapy in reducing the number of infusions to treat bleeds as compared with conventional therapies [10,13].

The phase 3 ASPIRE trial has further established the value of personalizing prophylaxis regimens to individual needs when required. Patients who were unable to achieve optimal dosing on the weekly or individualized regimens entered a modified treatment group in which their dosing could be further personalized to target trough levels or to be scheduled around activities. Patients on the modified regimen had a median ABR of 1.97 bleeding episodes per patient [11,12]. The proportion of patients experiencing 0 bleeds was 38.9% in the individualized prophylaxis group (median time on study = 80.6 weeks), 22.2% in the weekly prophylaxis group (median time on study = 78.5 weeks), and 23.5% in the modified prophylaxis group (median time on study = 79.5 weeks) [11,12].

With the availability of an effective prolonged half-life therapy, individuals may continue to transition from their present treatment to rFVIIIFc—episodic to prophylaxis, episodic to episodic, or prophylaxis to prophylaxis therapy—to realize the potential of reducing infusion frequency. It is unclear how these changes may influence formulary budgets. The objective of the budget impact analysis was to characterize the impact of including rFVIIIFc for hemophilia A on US private payer formulary budgets.

Methods

Model Structure and Target Population

A budget impact model specific to the United States was developed to estimate the economic impact of adding rFVIIIFc therapy for adult patients with hemophilia A from the perspective of a third-party private payer in the United States. The budget impact was assessed on the basis of therapy modality switching from conventional therapy to rFVIIIFc therapy. Three specific switching scenarios were evaluated: episodic to episodic, episodic to prophylaxis, and prophylaxis to prophylaxis therapy. The overall structure of the model, developed in Microsoft Excel, is shown in Figure 1.

The model is structured with annual cycles, a base year (2015), and two subsequent years (2016 and 2017). A top-down epidemiological approach was taken to estimate the cohort population size each year, with the population comprising prevalent cases of hemophilia A in adults, free from inhibitors, receiving treatment with recombinant therapy as either episodic or prophylaxis treatment. The mean age (34.5 years) and weight (74.29 kg) were taken from the ASPIRE trial [12]. The World Federation of Hemophilia's most recent US prevalence estimate of 8.18 per 100,000 males was applied [15]. In addition, the proportion of patients with hemophilia A who were severe was assumed to be 53% and the proportion of patients with severe hemophilia A with inhibitors was assumed to be 9% on the basis of the blood disorder registry of the Centers for Disease Control and Prevention [16]. A complete list of all model inputs is provided in Table 1.

The model includes only adult patients who have been previously treated with recombinant factor therapy; therefore, it was assumed that novel development of inhibitors in the model population during the time horizon of the model would be negligible [17–19], and factor treatment discontinuation due to inhibitors was not included in the model. It was also assumed that all severe patients would receive a recombinant-based factor therapy. General population mortality estimates obtained from

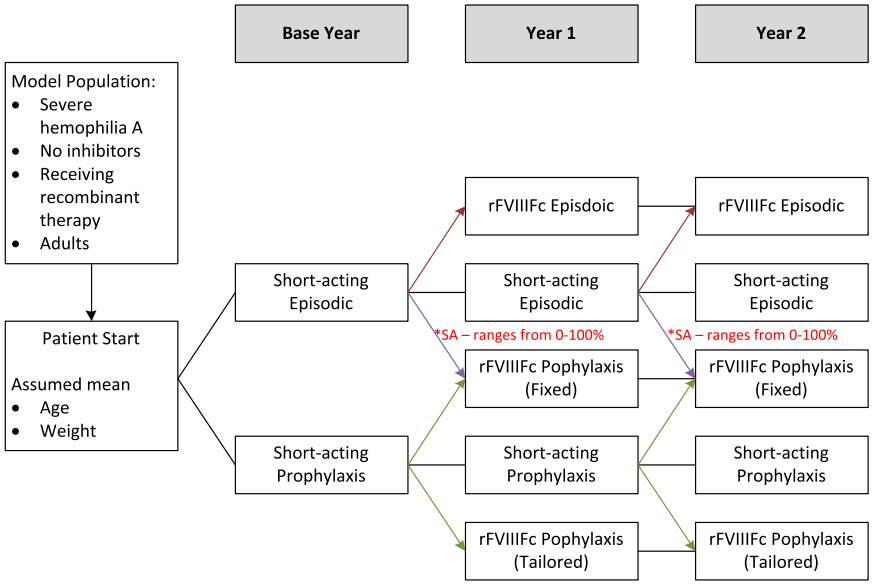

Fig. 1 – Budget impact model structure and patient flow. The budget impact model estimates the economic impact of adding rFVIIIFc therapy for an adult population with severe hemophilia A, over a 2-year time horizon. The model considers three therapy modality switching scenarios: episodic to episodic, episodic to prophylaxis, and prophylaxis to prophylaxis therapy. Sensitivity analyses were conducted regarding the assumptions of switching from episodic to prophylaxis, as this is the largest cost driver. FVIII, factor VIII; rFVIIIFc, recombinant FVIII Fc fusion protein; SA, sensitivity analysis.