Real World Dosing and Therapy Switching Patterns of rFVIII-Fc From Specialty Pharmacy Providers in the United States

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INTRODUCTION

- The first extended half-life rFVIII product in the US, rFVIII-Fc (Eloctate) provides a range of prophylactic regimens.
- For patients aged ≥ 6 years in the US, it is recommended that rFVIII-Fc patients begin prophylaxis with 50 IU/kg every 4 days. This dose can be adjusted based on patient response within a range of 25–60 IU/kg every 3–5 days. For patients < 6 years, prophylaxis may begin at 50 IU/kg twice weekly and adjusted according to patient response between 25–65 IU/kg at 3-5 day intervals, with more frequent or higher doses up to 80 IU/kg if required.[1]
- As real world experience is gained with rFVIII-Fc, it is important to understand prophylaxis dosing patterns and switching between FVIII and rFVIII-Fc. This may help understand costs associated with rFVIII-Fc therapy and identify appropriate treatment regimens for patients.

OBJECTIVE

- This study examined dosing and product switching patterns in patients treated with rFVIII-Fc.
- The first analysis examined prophylactic dosing patterns, including weekly dose and dosing infusion frequency.
- The second analysis examined time to switching from rFVIII-Fc back to rFVIII.

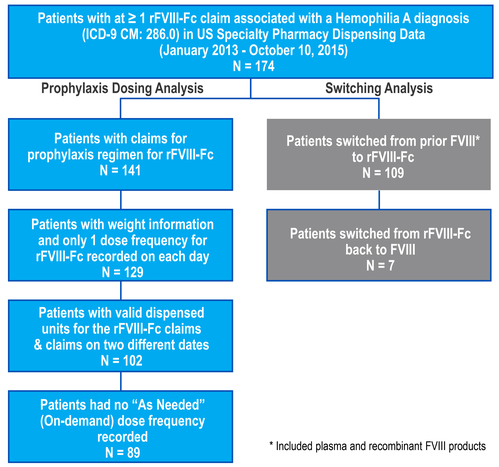
METHODS

- Patients with hemophilia A who were dispensed ≥ 1 rFVIII-Fc claim for prophylaxis were identified from specialty pharmacy data (January 2013–October 2015).
- For the dosing analysis, dispensed weekly dose (IU/kg) and distribution of dosing frequencies were assessed in patients with weight information and ≥ 2 rFVIII-Fc prophylaxis claims, who also did not receive on-demand treatment.
- Mean weekly prophylaxis doses were calculated based on dispensed units divided by number of days between claims and patient weight, then multiplied by 7. Dose from the last observed claim was excluded as number of days covered by that claim could not be calculated.
- For the switching analysis, patients were included if they switched from FVIII to rFVIII-Fc and subsequently switched back to FVIII. Switching patients were defined by ≥ 2 consecutive rFVIII-Fc claims followed by ≥ 2 consecutive FVIII claims (both with at least one claim for prophylaxis) and with no further rFVIII-Fc claims. Time to switch back to FVIII was examined using the Kaplan-Meier method.

RESULTS

- Sample selection for the prophylaxis dosing and switching analyses, respectively, are shown in Figure 1.

Figure 1: Schematic of Sample Selection for rFVIII-Fc Prophylaxis Dosing and Switching Analyses



* Included plasma and recombinant FVIII products

RESULTS continued

Prophylaxis Dosing Analysis of rFVIII-Fc

- The prophylaxis dosing analysis included 480 rFVIII-Fc claims for 89 patients (mean age 23.8 years; mean weight 68 kg; 62% severe hemophilia A). (Table 1)

Table 1: Characteristics of Haemophilia A Patients included in Prophylaxis Dosing Analysis

Demographics	All (N = 89)	Patients < 12 Years (N = 22)	Patients ≥ 12 Years (N = 67)
Age (years)			
Mean (SD)	23.8 (15.1)	6.2 (3.5)	29.6 (12.8)
< 12 years	24.7%	100%	NA
12-17 years	15.7%	NA	20.9%
≥ 18 years	59.6%	NA	79.1%
Weight (kg)			
Mean (SD)	68.1 (31.2)	28.6 (15.4)	81.1 (23.2)
Severity			
Mild	1.1%	0%	1.5%
Moderate	5.6%	9.1%	4.5%
Severe	61.8%	59.1%	62.7%
Unknown	31.5%	31.8%	31.3%

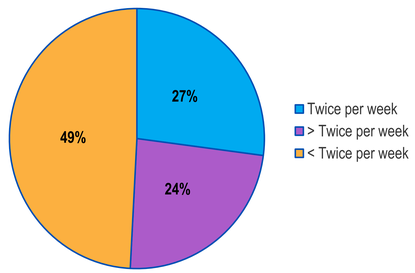
- Mean weekly prophylactic dose was 104 ± 79 IU/kg (median 89 IU/Kg). (Table 2) Mean weekly dose was highest and most variable in patients aged 0-11 years (139.7 ± 135.6 IU/kg) and lowest in patients aged ≥ 18 years (90.4 ± 43.9 IU/kg).

Table 2: Mean weekly prophylaxis rFVIII-Fc dose by age

		All Ages	0 –11 Years	12 –17 Years	≥ 18 Years
Claims (N)		480	119	94	267
Weekly prophylactic dose (IU/kg)	Mean (SD)	104 (79.4)	139.7 (135.6)	97.5 (38.2)	90.4 (43.9)
	Median	89.2	96.4	96.4	80
	Range (min-max)	19.1 – 1,119	40.8 – 1,119	19.1 - 241	25.1 - 282.5

- The majority of claims (62%) were prescribed for either every 4 days or 2 times/week; 24% of patients were prescribed > 2 doses/week. (Figure 1)

Figure 1: Dose Frequency for rFVIII-Fc Prophylaxis



Switching Analysis from rFVIII-Fc to FVIII

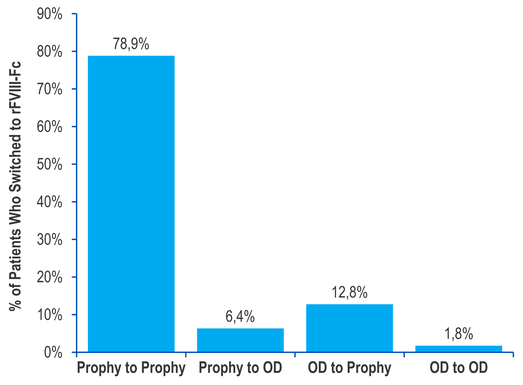
- The switching analysis included 109 patients who switched to rFVIII-Fc (mean age 23 years, mean weight 68kg, 57% severe haemophilia). (Table 3)

Table 3: Characteristics of Haemophilia A Patients For Switching Analysis

Demographics	All (N = 109)	Did not return to FVIII (N = 102)	Returned to FVIII (N = 7)
Age (years)			
Mean (SD)	23.2 (15.1)	23.2 (15.1)	14.3 (9.7)
< 12 years	27.5%	25.5%	57.1%
12-17 years	15.6%	15.7%	14.3%
≥ 18 years	56.9%	58.8%	28.6%
Weight (kg)			
Mean (SD)	67.9 (28.6)	68.0 (28.6)	66.7 (31.9)
Severity			
Mild	0.9%	1%	0%
Moderate	7.3%	6.9%	14.3%
Severe	56.9%	56.9%	57.1%
Unknown	34.9%	35.3%	28.6%

- Patients who returned to FVIII after rFVIII-Fc tended to be younger (mean 14 years), but this was not statistically significant using the Wilcoxon rank sum test (p = 0.09).
- 107 of the 109 patients initially switched from a recombinant FVIII product to rFVIII-Fc. All 7 patients who returned to FVIII after rFVIII-Fc, switched to a recombinant FVIII product.
- Most patients who initially switched from a prior FVIII to rFVIII-Fc switched from a prophylaxis regimen with FVIII to a prophylaxis regimen with rFVIII-Fc (78.9%). A further 12.8% of patients initially switched from on-demand treatment with FVIII to prophylaxis treatment with rFVIII-Fc. (Figure 2)
- Nine of the 109 patients (8.3%) who initially switched from a prior FVIII product, were subsequently treated on-demand with rFVIII-Fc.
- Of the 7 patients who returned to rFVIII after rFVIII-Fc, all switched from prophylaxis with rFVIII-Fc to prophylaxis with rFVIII. All but 1 of the 7 patients returned to the rFVIII product they had used before initially switching to rFVIII-Fc.

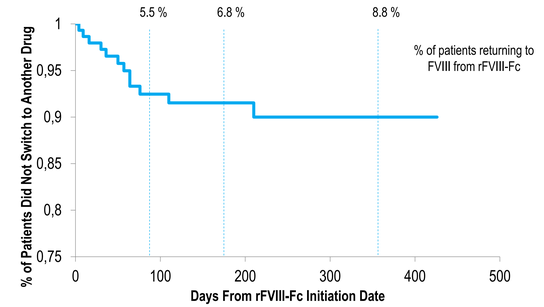
Figure 2: Proportion of Patients Switching to rFVIII-Fc by Prior FVIII Regimen and rFVIII-Fc Regimen**



** Percentages are rounded to nearest decimal place.

- Kaplan-Meier analysis indicated that 5.5%, 6.8%, and 8.8% of patients returned to another FVIII at 90 days, 180 days and 365 days respectively. (Figure 3)

Figure 3: Kaplan Meier Analysis of Patients Returning to FVIII After rFVIII-Fc



DISCUSSION AND LIMITATIONS

- The claims database used for this study is not inclusive of all specialty pharmacy providers and therefore may not be representative of the total US population with hemophilia.
- This analysis could be limited by inconsistent recording of treatment regimen (prophylaxis or on-demand), infusion frequency and disease severity in the claims data.
- Treatment selection with, and clinical response to, rFVIII-Fc may affect dosing patterns, but this was not investigated in this study due to lack of information in the claims data.
- Similarly, reasons for patient switching also could not be examined.

CONCLUSION

- Information on real world dosing continues to develop as more patients are prescribed rFVIII-Fc.
- Monitoring of dosing patterns as they develop, including the rate at which patients switch back to rFVIII from rFVIII-Fc, will assist clinicians and patients to better determine FVIII treatment options and regimens. Further research is required to better understand why patients switch between products.
- Understanding real world dosing and patterns of switching between FVIII products can also help payers to understand cost and clinical effectiveness implications for this new therapy.

REFERENCES

1. Eloctate Full Prescribing Information. Revised 01/2016. Biogen Inc. Cambridge, MA USA.

DISCLOSURES

*Author an employee of Baxalta ([1]Baxalta US, Inc., Cambridge, MA USA, [2]Baxalta US, Inc., Chicago, IL USA, [3]Baxalta US, Inc., Westlake Village, CA USA), now part of Shire.
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