Optimizing the Extended Half-life Recombinant Factor IX Regimen in Hemophilia B Prophylaxis

Lesley D'Albini PharmD, BCPS; Lesley.D'Albini@AccredoHealth.com, 913-634-9662
Accredo Inc., Warrendale, PA, USA

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ABSTRACT

Objective: Evaluate the impact of applying a factor specific evidence-based Regimen Optimization Algorithm at the dispensing specialty pharmacy level to assess dose and frequency of administration of extended half-life recombinant factor IX used as prophylaxis.

Methods: The electronic medical records of 85 patients using albutrepenonacog alfa or eftrenonacog alfa as prophylaxis in hemophilia B were retrospectively reviewed. The sample included data from inhibitor negative males, aged 18-89 years, using factor for a minimum of six consecutive quarters between 1-1-2021 and 12-31-2022. 170 discrete regimens were identified as evaluated per the factor specific Regimen Optimization Algorithm and included in the final sample. Data collected for each regimen included patient age, weight, extended half-life factor IX dose and interval originally prescribed, and the every 7-day equivalent regimen. For regimens failing the algorithm, additional review of pharmacist follow-up and prescriber engagement was performed. Patient reported bleeding events requiring infusion of additional factor IX as treatment were also collected and reviewed.

Summary: 41% (70/170) of reviewed regimens failed the factor specific Regimen Optimization Algorithm. Forty-eight (69%; 48/70) of these regimens met full criteria for prescriber engagement. Recommendations to adjust dose or interval were offered in the absence of prescriber provided clinical rationale in support of the original high dose regimen. Five recommendations to reduce the regimen, through either dose reduction or extension of the frequency of administration, were accepted by the prescriber. Follow-up revealed no change to the annualized bleed rate following the regimen reduction for any of these patients. Clinical rationale for the high dose regimen was obtained for the remaining forty-three; the most common being dosing to patient level pharmacokinetics, dose titration to efficacy defined as elimination of spontaneous bleeding episodes, and/or patient obesity.

Conclusions: Application of an evidence-based factor Regimen Optimization Algorithm can facilitate pharmacist-prescriber collaboration to achieve an extended half-life recombinant factor IX regimen that reduces patient infusion burden, maximizes clinical outcomes and provides payers with context around total cost of therapy.

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METHODS

Factor IX prophylaxis regimens are assessed by the specialist pharmacist per the *Regimen Optimization Algorithm-Extended Half-life Factor IX* protocol on receipt of all new or renewal prescriptions as part of the specialty pharmacy clinical model (figure 1). Findings of this review are documented in the patient medical record. On identification of an extended half-life (EHL) factor IX (FIX) regimen failing the algorithm, the prescriber is engaged to discuss regimen adjustments in alignment of evidence based guidelines and product labeling to patient level disease presentation. Outcomes from this peer-to-peer discussion are documented in the patient record – including memorialization of clinical rationale when the failed regimen remains unchanged.

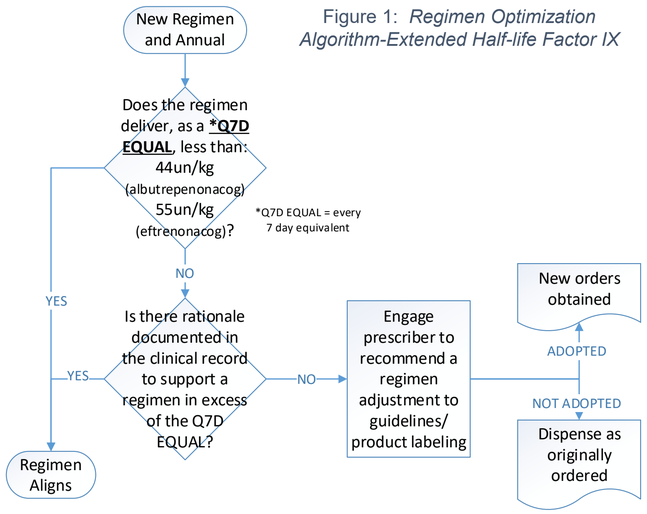


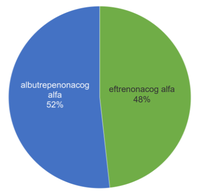
Figure 1: *Regimen Optimization Algorithm-Extended Half-life Factor IX*

Eligible regimens were reviewed for pass/fail status to guidelines/product labeling using the product specific specialty pharmacy proprietary algorithm.

Baseline data included: age, weight, body mass index (BMI), and dose and frequency of factor prophylaxis originally ordered. For failed regimens, documentation of prescriber engagement in recommendation of a dose or frequency adjustment was reviewed and outcome data collected. For adopted recommendations, detail around the regimen adjustment was collected. For non-adopted recommendations, clinical rationale in support of the failed regimen was collected.

RESULTS

Figure 2: Product Distribution



A total of 170 regimens were reviewed; 88 albutrepenonacog alfa and 82 eftrenonacog alfa (figure 2): two per patient, over six consecutive quarters, N=85 unique patients.

41% (70/170) of the reviewed regimens failed the algorithm (*Regimen Optimization Algorithm-Extended Half life Factor IX)* by delivering a Q7D EQUAL in excess of the evidence based product level threshold. Regimen failure rates were similar between the two products: 35% albutrepenonacog alfa and 48% eftrenonacog alfa (figure 3).

Figure 3: Regimen Alignment to Algorithm by Product

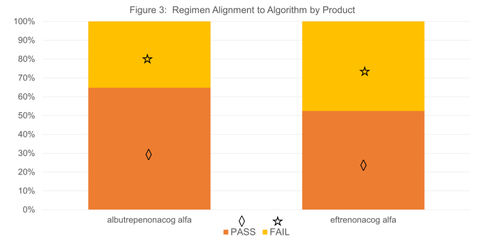
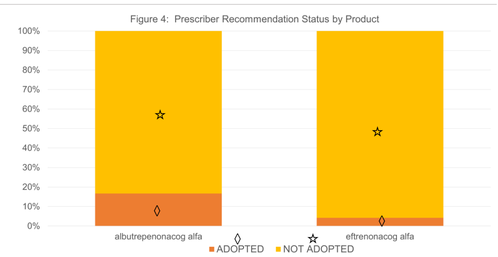
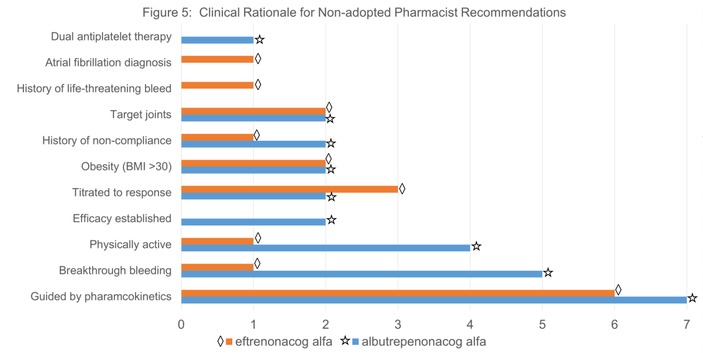


Figure 4: Prescriber Recommendation Status by Product



Prescriber engagement occurred with 69% (48/70) of failed regimens. The remaining 31% of failed regimens were cleared through review of documented clinical rationale justifying the higher Q7D EQUAL (i.e. patient level pharmacokinetics). For the majority of cases (76%; 19/25) in which a specialist pharmacist recommended an alternate regimen to more closely align to guidelines/product labeling, prescribers declined to adopt (figure 4). Figure 5 illustrates specific prescriber rationale for non-adoption of specialist pharmacist recommendations. Multiple rationale were documented for some regimens.

Figure 5: Clinical Rationale for Non-adopted Pharmacist Recommendations



Five of the 48 (10%) specialist pharmacist recommendations to prescribers were adopted; 4 albutrepenonacog alfa and 1 eftrenonacog alfa (table 1).

Table 1: Patient-Level Detail of Prescriber Adopted Recommendations

Drug	Dose (units)	Weight (kg)	un/kg	Interval	Q7D EQUAL (un/kg)	Baseline Annualized Bleed Rate	Clinical Pharmacist Recommendation	Dose (units)	Q7D EQUAL (un/kg)	Annualized Bleed Rate post adjustment
eftrenonacog alfa	13360	130.5	102	Weekly	102	0	Extend interval to every 10 days	13360	72	0
albutrepenonacog alfa	7000	90.7	77	Weekly	77	0	Extend interval to every 10 days	7000	54	0
albutrepenonacog alfa	7000	90.7	77	Every 10 days	54	0	Extend interval to every 14 days	7000	45	0
albutrepenonacog alfa	3500	71.2	49	Weekly	49	5	Dose reduction	3000	42	5
albutrepenonacog alfa	6225	83	75	Every 10 days	53	2	Dose reduction	4600	39	1

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3. D'Albini L, Dorholt M, Gallucci L. Optimizing maintenance dosing of emicizumab-kxwh as prophylaxis in hemophilia A: Dosing to product labeling while minimizing drug waste. *J Manag Care Spec Pharm.* 2023;29(1):47-57.

CONCLUSIONS

Application of an evidence-based factor Regimen Optimization Algorithm can facilitate pharmacist-prescriber collaboration to achieve an extended half-life recombinant factor IX regimen that reduces patient infusion burden, maximizes clinical outcomes and provides payers with context around total cost of therapy.

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