Section Editors: Lindsey Lyle and Wendy H. Vogel

# The Factor Approach: Coagulation Treatment Optimization and Recommendations (FACTOR)

SARA LEIDY, PharmD, BCOP, JORDAN SNYDER, PharmD, BCOP, and ZAHRA MAHMOUDJAFARI, PharmD, MBA, BCOP, FHOPA

From The University of Kansas Cancer Center, Westwood, Kansas

Authors' disclosures of conflicts of interest are found at the end of this article.

Correspondence to: Sara Leidy, PharmD, BCOP, 2330 Shawnee Mission Parkway, Westwood, KS 66205

E-mail: sbleidy@outlook.com

https://doi.org/10.6004/jadpro.2025.16.7.33



**Abstract**

Exogenous blood factor products, such as recombinant or human-derived factor VIIa, factor VIII, factor IX, and von Willebrand factor, are crucial for treating various bleeding disorders, but come with high risks and costs. Effective formulary management and development of institutional evidence-based guidelines for blood factor products are essential to maximize patient outcomes and minimize adverse events through an interprofessional approach. This article details the steps and considerations involved for the development of a blood factor product formulary and management at an academic medical center.

Exogenous blood factor products, such as recombinant or human derived factor VIIa, factor VIII, factor IX, and von Willebrand factor, are used in an array of acquired and congenital deficiencies, bleeding complications, and more. Federal funding, including hemophilia treatment centers, provides specialized care and has led to important randomized controlled trials, resulting in the approval of similar products (Arnall et al., 2023). Evidence-based medicine heavily relies on the impact a medication can make on clinical interventions, while rarely addressing the financial burden to patients or health systems (Owen et al., 2008). Additionally, international guidelines offer little assistance, as they generally promote the use of products that have been accepted by regulatory agencies with only consideration related to purity of the product (Srivastava et al., 2020). It is understandable that guidelines must maintain neutrality; however, it would be beneficial if more guidance was offered on formulary management. As such, there remains ambiguity with which blood factor products to use.

All approved products require close monitoring and dose titrations to adequately prevent or treat bleeding disorders while balancing the risk

of bleeding and thrombosis (Reardon et al., 2015). The most significant difference among these products is their economic burden; they represent a large aggregate expenditure with both direct and indirect costs (Amerine et al., 2015). Given the high risk and cost of these products, they have become a key area for stewardship initiatives. The benefits of blood factor product formulary management and implementation of an evidence-based guideline have previously been demonstrated (Arnall et al., 2023; Owen et al., 2008; Srivastava et al., 2020; Reardon et al., 2015; Amerine et al., 2015; Trueg et al., 2017). In developing a factor product formulary, patient outcomes can be maximized while adverse events are minimized through an interprofessional approach. Health systems should consider steps they can take to support the appropriate, safe, effective, and economical use of blood factor products.

## BACKGROUND

The University of Kansas Health System (TUKHS) is a 1,500-bed academic medical center that provides services to both acute and chronic medical conditions including inherited/acquired coagulopathies and acute bleeding/traumas that may require the use of blood factor products. Additionally, the system serves outpatient classical hematology patients and a large surgical population. Before August 2023, the system had no specific guidance on blood factor products in the setting of classical hematology. As a result, inconsistencies existed in the medication use process, such as product selection, dosing, frequency, and appropriate indications. It became pertinent to take steps to improve the processes surrounding blood factor products and ensure appropriate, safe, effective, and economical use. While extensive literature exists to support blood factor product formulary management and implementation of evidence-based guidelines, there is limited information on methods to operationalize these efforts. This article details the steps taken by the pharmacy team to make key practice changes for blood factor products at a single academic center.

## DEVELOPMENT OF A BLOOD FACTOR PRODUCT FORMULARY

The development and implementation of a blood factor product formulary requires many phases, including analysis, creation, implementation, and education.

### Analysis

Prior to the implementation of the blood factor formulary, selection and initiation were typically carried out by a provider, most commonly a board-certified hematology physician or advanced practice provider on the classical hematology consult service. This order was received by the inpatient board-certified oncology pharmacist, who would query the dispensing pharmacy to assess available vial size to comprise the patient dose. The verifying pharmacist would then adjust the order to reflect the appropriate number of units. As such, it was imperative to engage with multiple stakeholders including, but not limited to, managers and front-line staff, the interprofessional team of providers, pharmacists, and nurses, as well as staff from purchasing/supply chain, laboratory, and information technology. These individuals were informed of the goal to create a blood factor product formulary and their perceived role in development of these efforts.

To identify improvement opportunities, information was collected from established blood factor product programs, feedback from the interprofessional team at TUKHS, and a review of safety events and expenditures. Feedback was solicited via an email survey to all individuals involved in the blood factor product medication use process, including what currently worked well, opportunities for improvement, identified issues, concerns related to the development of a blood factor product formulary, and any specific recommendations based on experience. Safety events from a 12-month period were reviewed to understand trends and to help justify the time needed to develop and implement a blood factor product formulary. Finally, data on 6 months of blood factor product usage from April 1, 2022, to September 30, 2022, for both inpatient and outpatient settings were evaluated. A review of primary literature showed a lack of head-to-head evidence that limits the ability to assess efficacy and safety between available products. Therefore, it was imperative to have a strong understanding of the costs to the institution. Consequently, a comparative financial analysis of blood factor products not being utilizing was also completed. From this,

**Table 1. SWOT Analysis**

| Strengths | Weaknesses |
|---|---|
| • Ease of blood factor product fridge and inventory binder use | • Lack of standardization and guidance<br>• Delay in care with need to order variety of products not in stock |
| **Opportunities** | **Threats** |
| • Standardization of blood factor products used, monitoring, dosing, communication, ordering ownership<br>• Guidance to promote consistency of pieces standardized<br>• Improve orderability through decreasing product options and streamlined order sets and beacon plans<br>• Use of electronic inventory system | • Expansive TUKHS campus with various locations could challenge implementation<br>• Heterogeneity in ordering team workflows and comfortability with blood factor products |

a strengths, weaknesses, opportunities, and threats (SWOT) analysis was performed (Table 1).

## Creation

To begin constructing the blood factor product formulary, a summary document was created (Figure 1). This document was reviewed in partnership with classical hematology providers. One formulary product was selected for each class of blood factor product. Certain products with extended half-life and monoclonal antibodies were restricted to outpatient use only, given their limited use in an acute setting. In addition to the selection of products for the blood factor product formulary, a blood factor product algorithm was created to help guide the appropriate use of these products (Figure 2). The algorithm was reviewed and approved by hematologists and the Pharmacy and Therapeutics subcommittee at TUKHS and is available health-system wide. The institution created additional guidance related to the diagnosis of the disease states found in the algorithm, as well as how to coordinate outpatient and operating room ordering.

## Implementation

Implementation of the blood factor product formulary and associated algorithm was simple. The resources were uploaded to the institution's web-based document management system that allows on-demand access and houses important policies

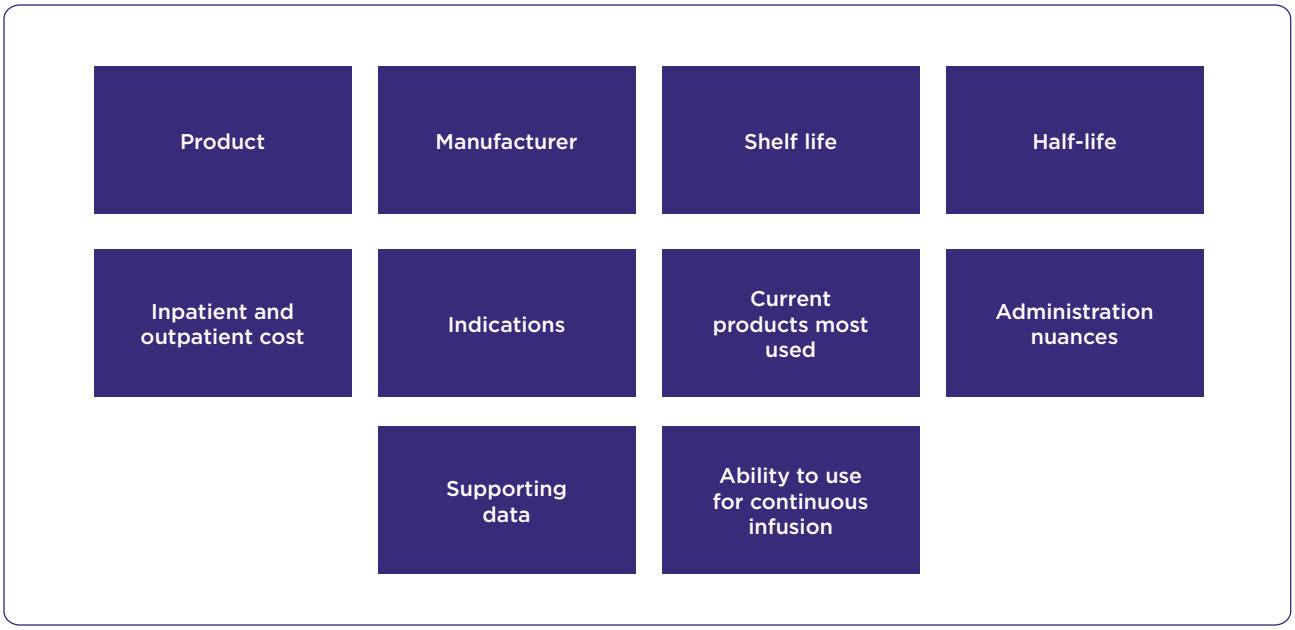


**Figure 1.** Blood factor product comparison.

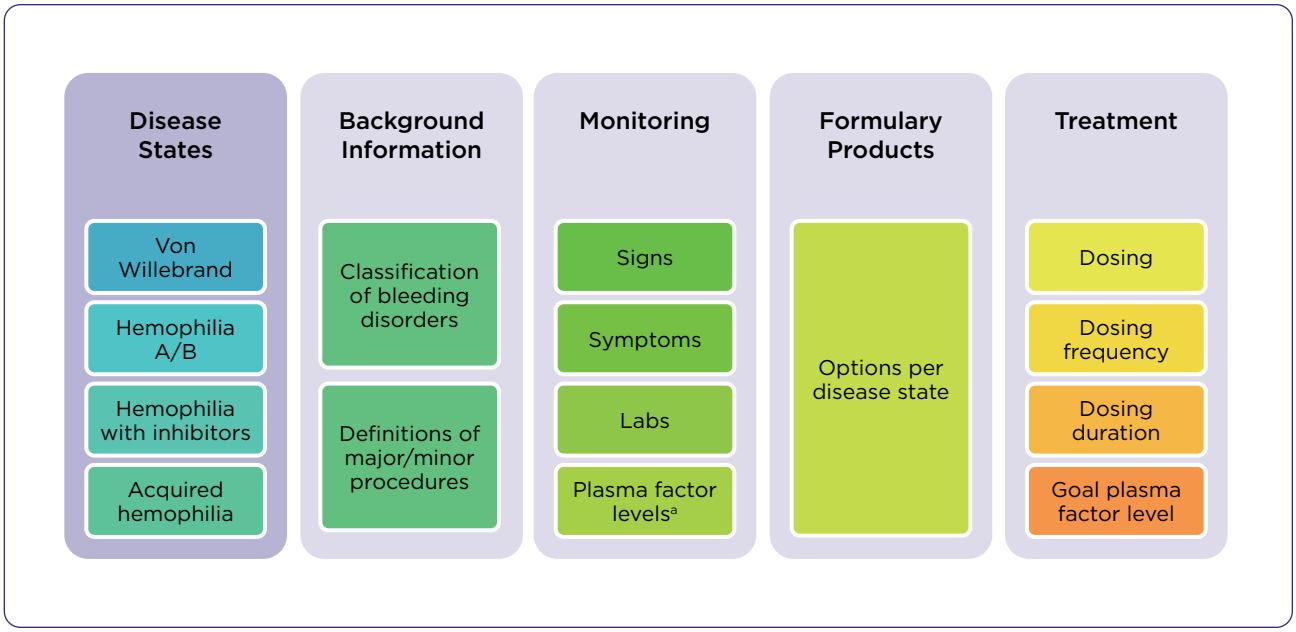


**Figure 2.** Blood factor product algorithm.
[a]Plasma factor levels guidance should include indications for troughs and peaks, timing of levels, frequency, and expected increase in plasma factor level per blood factor product.

and procedures. Existing policies and guidelines were reviewed to ensure they were concurrently updated. We worked to guarantee that appropriate drug entries for selected formulary products were available in the electronic medical record. Non-formulary products were able to be selected as an alternative only for an appropriate reason determined by the management team via a standardized submission form. Ordering processes and workflow for nurses, providers, and pharmacists did not change with the implementation of this blood factor product formulary and algorithm.

## Education

Education and detailed follow-up are major contributors to compliance and success for blood factor product stewardship (Owen et al., 2008). To supplement guidelines and clinical practice experience, the institution provided the opportunity for the lead pharmacist on this project to complete the American Society of Health-System Pharmacists classical hematology certificate. This proved to be instrumental to the success of the project. Additionally, the institution provides a yearly lecture opportunity regarding factor product management to pharmacy practice residents and pharmacists. It is essential to have a strong base knowledge in order to initiate a project related to blood factor products in the classical hematology space. Given there were no adjustments to ordering processes or workflows, no additional education was provided surrounding these processes.

## Understanding the Impact

As non-factor therapies emerge, blood factor products remain vital for acute bleeds, breakthrough events, and inhibitor management, emphasizing the continued importance of factor stewardship. Blood factor stewardship programs have demonstrated improved outcomes in patients receiving blood factor concentrates with significant cost savings. Depending on the setting, a 45% to 49% reduction in the number of blood factor doses administered has been observed, despite a similar or increased volume of treated patients, resulting in estimated cost savings ranging from $100,000 to $4 million. These interventions had no impact on patient outcomes (Owen et al., 2008; Reardon et al., 2015; Amerine et al., 2015).

Another program reported the results of a pharmacist-directed blood factor stewardship program targeting off-label utilization designed to

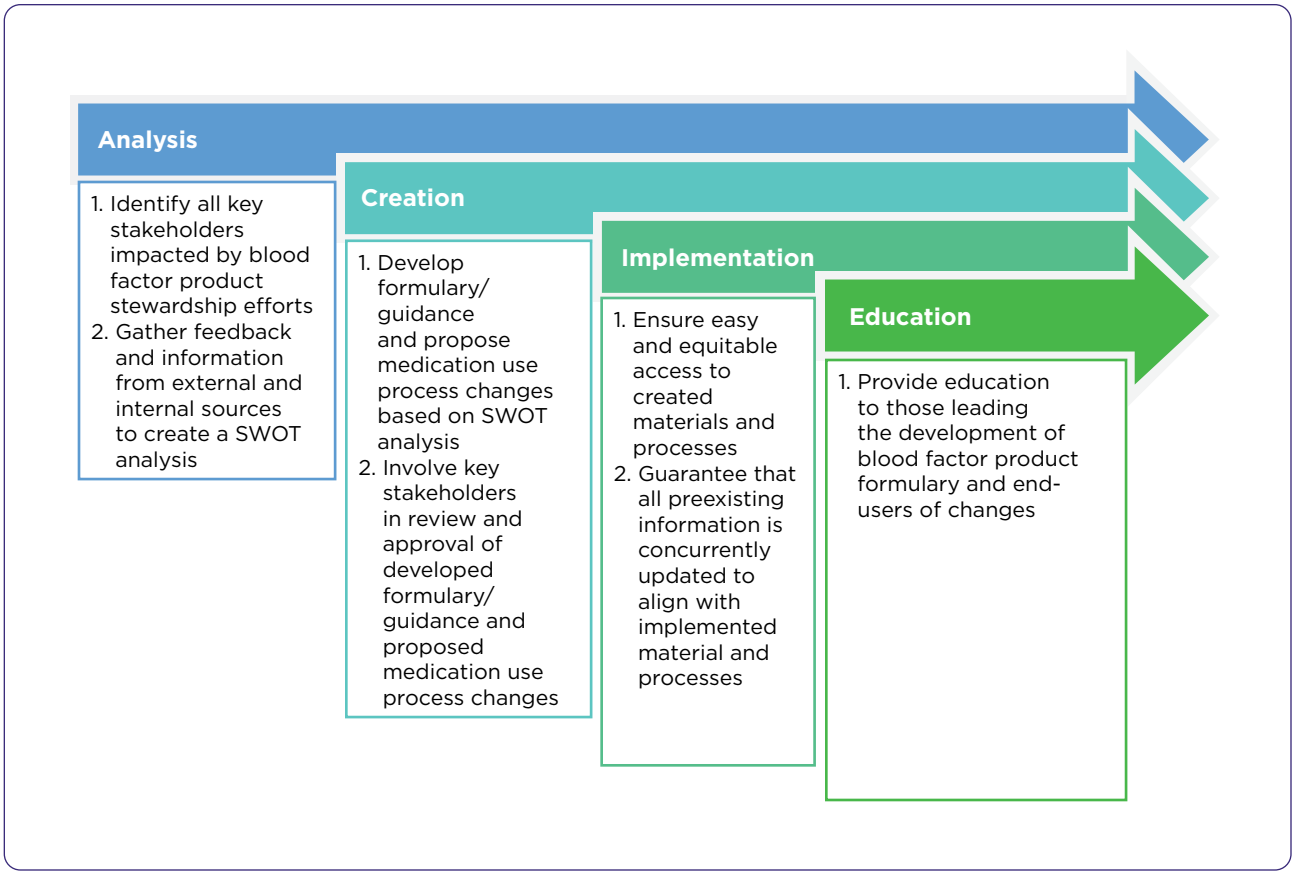


**Figure 3.** Blood factor product stewardship initiatives summary.

limit use according to established organizational guidelines in high-risk populations. An annual cost savings of $375,539 was achieved, primarily through a significant reduction in recombinant factor VIIa and avoidance in high-risk patients (Trueg et al., 2017).

These papers offer valuable insights and a strong foundation for key initiatives. However, full implementation may be challenging due to scope and resource demands. Institutions should tailor efforts to their needs or adopt a stepwise approach to blood factor stewardship. Anecdotally, the algorithm has led to streamlined efforts and efficiencies within our health system. We routinely evaluate our blood factor formulary process and adjust based on recent literature and cost. A formalized evaluation will be completed at 2 years post implementation to verify the positive anecdotal evidence. Building on the initial efforts, sustained progress has relied on multidisciplinary collaboration among board-certified hematologists, advanced practice providers, and interprofessional staff. These initiatives have enabled ongoing optimization of blood factor practices, with advanced practice providers playing key roles in problem-solving, workflow efficiency, and patient and staff education. TUKHS remains committed to engaging the full care team in continued improvement, evaluation, and future endeavors for blood factor product stewardship.

## CONCLUSION

The development and implementation of a blood factor product formulary results in standardized use of high-risk, high-cost products, enhancing patient outcomes and minimizing adverse effects. This article highlights the phases and framework needed to ensure the appropriate use of blood factor products (Figure 3). An interprofessional approach to manage complex medication therapies can improve health-care delivery from a clinical and economic perspective.

## Disclosure

Dr. Mahmoudjafari, PharmD, MBA, BCOP, FHOPA serves as an advisory board participant for Genmab, Pfizer, Sanofi, and Genentech. The other authors have no conflicts of interest to disclose.

## References

Arnall, J., Moore, D., Michael, M., Wolcott, M., & Cowgill, N. (2023). Measuring the impact of a pharmacist-driven blood factor education program: A prospective, single-center observational study. *Hospital Pharmacy, 58*(3), 282–288. https://doi.org/10.1177/00185787221137901

Owen, P., Golightly, L., MacLaren, R., Ferretti, K., & Badesch, D. (2008). Formulary management of recombinant factor VIIa at an academic medical center. *Annals of Pharmacotherapy, 42*(6), 771–776. https://doi.org/10.1345/aph.1L047

Srivastava, A., Santagostino, E., Dougall, A., Kitchen, S., Sutherland, M., Pipe, S. W., Carcao, M.,...Pierce, G. F. (2020). WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia, 26*(Suppl. 6), 1–158. https://doi.org/10.1111/hae.14046

Reardon, D. P., Atay, J. K., Ashley, S. W., Churchill, W. W., Berliner, N., & Connors, J. M. (2015). Implementation of a hemostatic and antithrombotic stewardship program. *Journal of Thrombosis and Thrombolysis, 40*(3), 379–382. https://doi.org/10.1007/s11239-015-1189-3

Amerine, L. B., Chen, S. L., Daniels, R., Key, N. S., Eckel, S. F., & Savage, S. W. (2015). Implementation of a factor stewardship program to optimize care in hemophilia and bleeding disorders. *American Journal of Health-System Pharmacy, 72*(18), 1579–1584. https://doi.org/10.2146/ajhp140722

Trueg, A. O., Lowe, C., & Kiel, P. J. (2017). Clinical outcomes of a pharmacy-led blood factor stewardship program. *American Journal of Therapeutics, 24*(6), e643–e647. https://doi.org/10.1097/MJT.0000000000000371