Shifting Treatment Perspectives in Polycythemia Vera

Real-World Experience with Ropeginterferon Alfa-2b

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Executive Summary

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm associated with increased thrombotic risk, symptom burden, and the potential for long term disease progression. Historically, treatment has centered on phlebotomy and cytoreductive therapy with hydroxyurea (HU), with a primary focus on hematocrit control and prevention of vascular events.[1] In recent years, interferon based therapies, including BESREMi® (ropeginterferon alfa-2b), have emerged as an important option with the potential to offer deeper and more durable disease control, including reduction in JAK2 allele burden.[2,3]

As clinical evidence and guideline inclusion have evolved, so too has interest in integrating ropeginterferon alfa-2b earlier in the treatment paradigm.[4] To better understand how this shift is translating into real world practice, multidisciplinary focus groups were conducted with physicians, advanced practice providers, and pharmacists across community and academic settings, supported by pre-survey insights. The goal was to identify current utilization patterns, as well as practical barriers and enablers to broader adoption.

Across both focus groups, clinicians demonstrated strong awareness of ropeginterferon alfa-2b and increasing confidence in its clinical role, particularly for younger patients and those requiring long term disease management.[2,3] At the same time, hydroxyurea continues to serve as the default first line therapy in many settings, largely due to its simplicity, familiarity, and ease of use. In contrast, initiating ropeginterferon alfa-2b often requires additional coordination related to prior authorization, reimbursement, and specialty pharmacy workflows, which can influence treatment selection in busy clinical environments.

Importantly, findings suggest that variability in adoption is less about clinical hesitation and more about differences in infrastructure, workflow integration, and patient experience. Practices with medically integrated pharmacy support, clear education pathways, and proactive follow up processes reported more streamlined implementation and greater comfort with use. These insights highlight the opportunity to expand adoption by focusing on operational efficiencies and team-based care models already familiar to many oncology practices.

Patient considerations also play a meaningful role in treatment decisions. While some patients prefer the convenience of oral therapy, others are receptive to less frequent dosing when appropriate education and support are provided. At the time of the focus groups, the prefilled syringe formulation presented complexities related to administration and dose preparation. Since completion of these discussions, the FDA has approved a pen device for ropeginterferon alfa-2b[5], an advancement that may simplify administration, reduce medication waste, and improve both the patient and provider experience. Future real-world experience will help define its impact on treatment adoption and workflow.

Encouragingly, a shift in clinical mindset is already underway. Many clinicians described increasing use of ropeginterferon alfa-2b earlier in the disease course, particularly as familiarity grows and workflows are optimized. This evolution reflects a broader focus on long term disease control and patient-centered outcomes, balanced with practical considerations such as access and tolerability.[2,3]

Overall, the findings point to a clear opportunity to better align clinical intent with real world practice. By addressing implementation workflow, enhancing education, and supporting consistent strategies, practices can more easily incorporate ropeginterferon alfa-2b into PV management. In this context, the conversation is evolving from whether to use interferon-based therapy to how to use it most effectively within existing care delivery models.

Background & Clinical Context

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm driven in the majority of cases by activating mutations in JAK2, resulting in uncontrolled erythrocytosis and an increased risk of thrombosis, disease related symptoms, and long term complications including myelofibrosis and acute leukemia.[1] The primary goals of therapy have historically focused on reducing thrombotic risk through hematocrit control, most commonly achieved with phlebotomy and cytoreductive therapy in higher risk patients.[1]

Hydroxyurea (HU) has long served as the standard first line cytoreductive agent due to its ease of use, rapid hematologic control, and broad familiarity across oncology practices.[4] However, limitations of HU have become increasingly recognized, including intolerance, resistance, and a lack of disease modifying activity. As understanding of PV biology has evolved, there has been growing interest in therapies that not only control blood counts but also address the underlying disease process.

Interferon based therapies have emerged as a key option in this context. Ropeginterferon alfa-2b, a long acting, monopegylated interferon, offers a differentiated dosing schedule and has demonstrated the ability to achieve sustained hematologic responses and reduce JAK2 allele burden over time.[2,3] These properties have positioned interferon therapy as a potential approach for long term disease control, particularly in younger patients and those for whom durability of response is a priority. As a result, clinical guidelines have increasingly incorporated interferon-based options, including ropeginterferon alfa-2b, into treatment algorithms for PV. Notably, the National Comprehensive Cancer Network® (NCCN®) Guidelines list ropeginterferon alfa-2b as a preferred first-line cytoreductive treatment option for both low-risk and high-risk symptomatic patients with PV.[4]

Recent and ongoing clinical studies continue to expand the evidence base for ropeginterferon alfa-2b across different patient populations and treatment settings. The PROUD-PV and CONTINUATION-PV studies established long-term efficacy and safety, supporting its role as a durable treatment option.[2] Building on this foundation, newer studies are evaluating earlier intervention strategies and broader use across the disease continuum. For example, the Low-PV study (NCT05481151) is exploring the use of ropeginterferon alfa-2b in patients with low-risk PV, reflecting growing interest in earlier disease modification rather than delayed cytoreduction.[6] Beyond PV, the phase 3 SURPASS-ET trial demonstrated superior efficacy of ropeginterferon alfa-2b compared with anagrelide in patients with hydroxyurea-resistant or -intolerant essential thrombocythemia, further supporting the role of interferon-based therapy across myeloproliferative neoplasms.[7] Complementing the phase 3 SURPASS-ET trial, EXCEED-ET confirmed the efficacy, molecular activity, and favorable safety profile of ropeginterferon alfa-2b in a broader North American population with ET, including both treatment-naïve and previously treated patients.[8]

These developments highlight an important shift in the management of PV. While traditional approaches have prioritized short term hematologic control, there is increasing emphasis on long term outcomes, including symptom burden, quality of life, and potential modification of disease trajectory. At the same time, translating these advances into routine clinical practice introduces new considerations related to treatment selection, care delivery, and patient experience.

Within this evolving landscape, understanding how ropeginterferon alfa-2b is currently being used, and what factors influence its integration into practice, is critical. The following sections examine real world insights from multidisciplinary clinicians to better characterize current treatment patterns, identify implementation challenges and emerging best practices, and highlight opportunities to optimize care for patients with PV.

Methodology

To better understand real world utilization of ropeginterferon alfa-2b in polycythemia vera, a qualitative research approach was conducted using a combination of pre-survey data and moderated focus group discussions. The objective was to capture multidisciplinary perspectives on current treatment patterns, barriers to adoption, and practical strategies for implementation across diverse oncology care settings.

Study Design

This initiative consisted of two structured virtual focus groups conducted in April 2026, supplemented by a pre-meeting survey distributed to all participants. The discussions were designed to explore both current clinical practice and future considerations for integrating ropeginterferon alfa-2b into routine care.

- Focus Group 1 emphasized current state challenges, including treatment positioning, access barriers, and workflow considerations
- Focus Group 2 focused on evolving practice patterns, optimization strategies, and opportunities to improve implementation
- Each session followed a standardized moderator guide to ensure consistency while allowing for open discussion and peer exchange.

Participants

Participants were recruited through NCODA and represented a multidisciplinary group of oncology stakeholders involved in the management of PV, including:

- Medical oncologists and hematologists
- Advanced practice providers
- Clinical pharmacists and specialty pharmacy leaders

Both community-based and academic practices were represented, enabling a range of perspectives reflecting variability in infrastructure, patient populations, and access models.

Pre-Survey Assessment

Prior to the focus groups, participants completed a structured survey designed to quantify baseline perceptions and experiences related to ropeginterferon alfa-2b. Survey topics included:

- Current positioning within treatment pathways
- Perceived barriers to earlier use
- Injection and administration considerations
- Insurance and access challenges
- Adverse event management and treatment persistence
- Alignment with NCCN guidelines

Survey results were used to inform discussion prompts and identify key areas of focus for deeper exploration during the sessions.

Data Collection and Analysis

Focus group discussions were recorded, transcribed, and thematically analyzed to identify recurring patterns and insights. Responses were deidentified and aggregated to ensure confidentiality while preserving the authenticity of participant perspectives.

A qualitative thematic analysis approach was used to categorize insights across key domains, including:

- Treatment landscape and decision making
- Operational and access barriers
- Patient experience factors
- Implementation strategies and best practices

Findings from both focus groups were integrated with pre-survey results to develop a comprehensive view of current practice and emerging trends.

Update Since Completion of the Focus Groups

The focus groups and pre-survey summarized in this white paper were conducted prior to FDA approval of the BESREMi Pen™ device[5]. Participant comments regarding treatment administration, injection experience, and medication preparation therefore reflect experience with the prefilled syringe formulation. Where appropriate, discussion sections note how the newly approved pen device may influence future implementation and patient experience.

Current Landscape

The treatment landscape for PV continues to reflect a balance between established clinical practice and emerging therapeutic options. While advances in disease understanding and guideline updates have expanded available treatments, real world utilization remains anchored in long standing approaches, with variability across practice settings.[1,4]

Hydroxyurea (HU) remains the most commonly used first line cytoreductive therapy in PV, particularly in community oncology settings.[1,4] Its widespread use is driven by several practical factors, including familiarity among providers, ease of prescribing, rapid hematologic control, and minimal administrative burden. As a result, HU is often the default starting point for patients requiring cytoreduction beyond phlebotomy.

This pattern persists even as treatment goals evolve. While clinicians are increasingly aware of the importance of long-term disease control and symptom management, treatment decisions are frequently influenced by operational considerations favoring therapies that can be initiated quickly and with minimal complexity.

Positioning of Ropeginterferon Alfa-2b

Ropeginterferon alfa-2b is recognized across practices as an important therapeutic option in PV, with growing confidence in its clinical role. However, its positioning within treatment pathways varies considerably.

In many practices, particularly those with less established infrastructure for specialty therapies, ropeginterferon alfa-2b is most commonly introduced after HU intolerance or resistance. In this context, it is viewed as a second line option aligned with guideline recommendations and used in patients requiring an alternative cytoreductive strategy.[4]

At the same time, a subset of clinicians, more frequently in academic settings, are incorporating ropeginterferon alfa-2b earlier in the treatment course. These providers are more likely to consider it as an initial therapy in select patient populations, particularly younger individuals or those for whom long term disease management is a priority.

This variability highlights an important dynamic within the current landscape. Awareness of ropeginterferon alfa-2b is high, and its clinical value is generally accepted. However, the timing of its use is influenced by practice environment, provider experience, and available support systems.

Clinical guidelines, including those from NCCN, are widely recognized as the standard for PV management and are referenced across practice settings . However, their influence

on real time decision making is variable. While providers report general adherence to guideline principles, implementation is often indirect, particularly in the absence of embedded clinical pathways within electronic health records.

In many cases, treatment decisions are guided by a combination of clinical judgment, prior experience, and practical considerations rather than direct consultation of guidelines at the point of care. This can contribute to variability in how newer therapies, including ropeginterferon alfa-2b, are incorporated into routine practice.

Barriers to Adoption

While awareness and clinical confidence in ropeginterferon alfa-2b are increasing, its integration into routine PV management remains uneven. Insights from focus group participants consistently indicate that barriers to adoption are primarily operational and practical in nature, rather than driven by concerns about clinical efficacy. These barriers span access, workflow, patient experience, and treatment administration, and together shape real world treatment decisions.

Access related barriers represent one of the most consistently cited challenges across practice settings. Participants described prior authorization requirements, step therapy protocols, and variable payer policies as factors that can delay treatment initiation and influence therapy selection.

Although clinicians generally reported that access to ropeginterferon alfa-2b is achievable, initiating therapy often requires substantial coordination and administrative effort. This creates a meaningful contrast with HU, which can typically be prescribed without delay. As one participant noted, the difference is not whether access is possible, but the time and effort required to achieve it.

Financial considerations also play a role, particularly for patients covered under Medicare. Out of pocket costs and reimbursement uncertainty can create additional complexity, requiring navigation of patient assistance programs or alternative funding pathways.

Workflow and Operational Complexity

Operational burden is a central theme influencing adoption. Initiating ropeginterferon alfa-2b often requires coordination across multiple stakeholders, including providers, nursing teams, and pharmacists. This includes documentation, prior authorization submission, patient education, and follow-up planning.

Participants highlighted the contrast between this process and the simplicity of prescribing HU, noting that ropeginterferon alfa-2b initiation may require hours of coordination compared to minutes for more established therapies. In busy oncology practices, where efficiency is critical, this difference can significantly influence treatment selection.

Additional workflow challenges include fragmentation across care settings. In some models, the team responsible for patient education is not directly connected to the dispensing pharmacy, creating gaps in continuity and communication. Variability in specialty pharmacy processes further contributes to inconsistency in patient experience and provider confidence.

Provider Familiarity and Patient Experience

Provider experience and established prescribing habits remain influential. HU has been used for decades and is

Key Barriers and Practice-Based Solutions for Ropeginterferon Alfa-2b Implementation

	Common Barrier Identified	Practice-Based Solution
Access & Reimbursement	Prior authorization complexity	Integrated pharmacy and reimbursement support
Workflow Integration	Administrative coordination burden	Standardized initiation workflows
Provider Familiarity	Reliance on established HU prescribing patterns	Increased multidisciplinary experience and education
Patient Acceptance	Injection hesitancy and administration concerns	Structured education and expectation setting
Monitoring & Follow Up	Inconsistent longitudinal follow up	Early check-ins and proactive monitoring
Care Coordination	Fragmentation across care teams and pharmacies	Multidisciplinary care models/Medically Integrated Pharmacy
Administration	Prefilled syringe complexity and medication waste	Implementation of the newly approved pen device

Table 1. Focus group participants identified several operational, workflow, and patient-related challenges that may influence adoption of ropeginterferon alfa-2b in routine practice. Participants also described practical strategies and care delivery approaches that may help support more efficient initiation, coordination, and long-term management across diverse oncology settings.

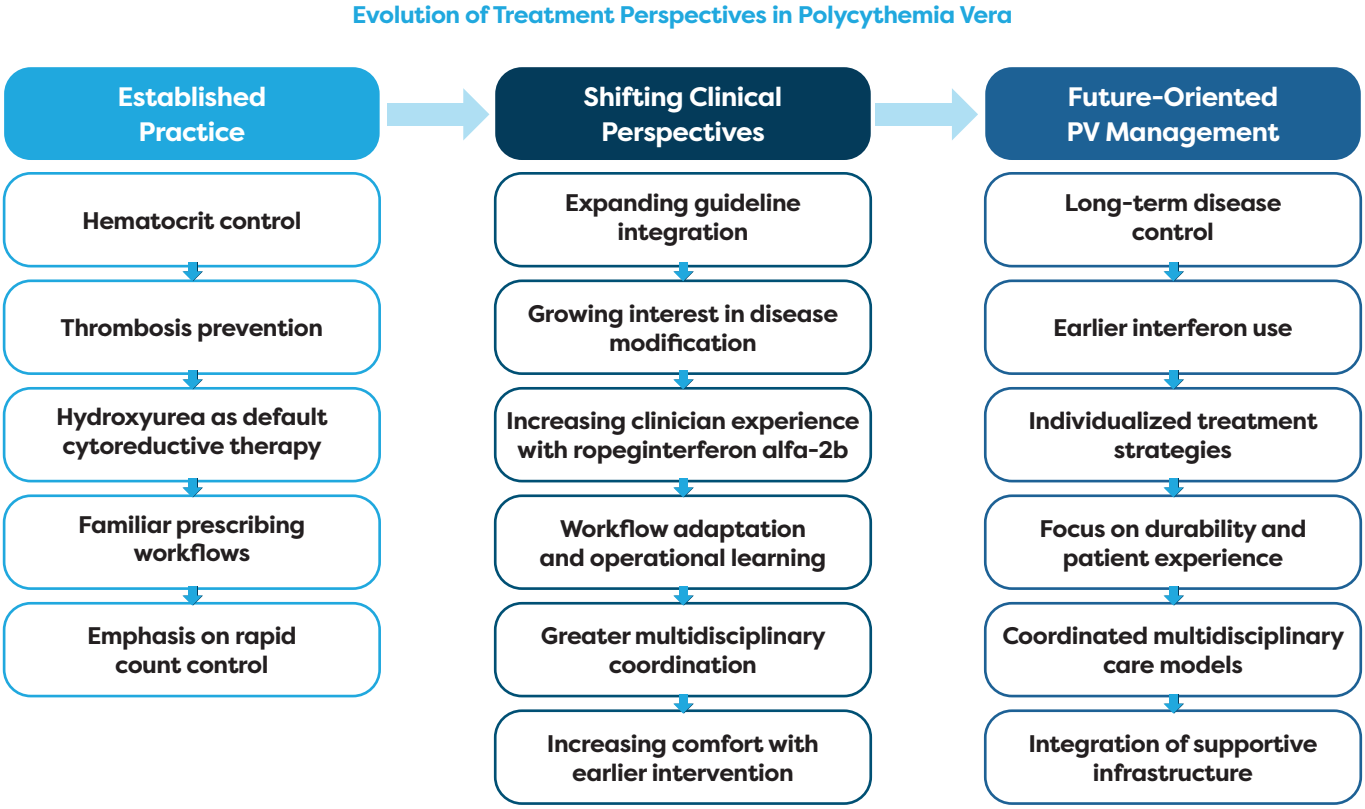


Figure 1: Focus group participants described an ongoing shift in PV management from established approaches centered on rapid hematologic control toward more proactive and individualized long-term management strategies. Increasing familiarity with ropeginterferon alfa-2b, expanding guideline integration, and improvements in operational workflows are contributing to broader consideration of interferon-based therapy earlier in the disease course.

deeply embedded in clinical practice, supported by familiarity, perceived reliability, and straightforward logistics. In contrast, ropeginterferon alfa-2b may be less familiar to some providers, particularly in community settings where exposure to newer therapies may be more limited.

Participants also noted that the absence of PV specific treatment pathways within electronic health records can reinforce reliance on habitual prescribing patterns. Without embedded guidance at the point of care, providers are more likely to default to therapies that are easier to access and implement, even when aware of alternative options.

Patient related factors are another important driver of treatment decisions. Across both focus groups, injection hesitancy emerged as a consistent barrier. Many patients express a preference for oral therapy, particularly when faced with the choice between a familiar oral agent and a self-administered injectable treatment.

This preference is often more pronounced among older patients, who may have concerns related to dexterity, vision, or lack of support at home. In addition, logistical considerations such as refrigeration requirements, travel, and the need for initial training can influence willingness to initiate therapy.

At the same time, participants noted that patient perspectives are not uniform. With appropriate education and support, some patients are receptive to less frequent dosing and the potential for long term disease control. This highlights the importance of communication and expectation setting in shaping patient acceptance.

The newly approved ropeginterferon alfa-2b pen device may help mitigate some of the administration-related barriers described by participants, particularly those related to self-injection confidence, dose preparation, and patient education. Ongoing real-world experience will help clarify its impact on treatment adoption, adherence, and clinical workflow.

Despite the operational and practical barriers outlined above, findings from both focus groups point to a clear and encouraging shift in the treatment landscape for PV. Clinicians across settings described evolving perspectives on ropeginterferon alfa-2b, with increasing comfort, earlier use in select patients, and growing alignment with long term disease management goals.

Key Success Factors Supporting Effective Ropeginterferon Alfa-2b Implementation

Figure 2: Focus group findings suggest that successful implementation of ropeginterferon alfa-2b depends on coordinated operational and clinical support across the care continuum. Practices reporting the greatest success typically described integrated infrastructure, proactive monitoring, multidisciplinary collaboration, and consistent patient engagement strategies working together to support initiation, adherence, and long-term persistence.

Earlier Integration and Evolving Treatment Perspectives

One of the most notable trends is the movement toward earlier integration of ropeginterferon alfa-2b in the treatment course. While historically positioned after HU intolerance or resistance, a growing number of clinicians, particularly in academic and specialty focused practices, are considering its use in earlier lines of therapy.

This shift is most evident in younger patients and those with longer anticipated disease trajectories, where treatment decisions are increasingly influenced by long term outcomes rather than short term hematologic control alone. In these cases, ropeginterferon alfa-2b is viewed as a proactive strategy to support sustained disease management.

Participants described a broader evolution in how PV is managed, reflecting a transition from a primarily reactive approach to a more strategic, long-term perspective. There is increasing recognition that treatment decisions made early in the disease course may influence long term outcomes, including symptom burden, treatment durability, and overall quality of life.

This shift is accompanied by greater openness to incorporating therapies that may require more initial coordination but offer potential benefits over time. As familiarity with ropeginterferon alfa-2b increases, clinicians are becoming more comfortable navigating its use and integrating it into individualized treatment plans.

Increasing Experience and Operational Maturity

Experience was consistently identified as a key driver of adoption. Clinicians who had successfully initiated and managed patients on ropeginterferon alfa-2b reported increased confidence in both its efficacy and tolerability. This, in turn, influenced their willingness to consider it earlier in subsequent patients.

Importantly, this trend was not limited to physicians. Pharmacists, advanced practice providers, and nursing teams also described increased comfort as workflows became more established and familiarity with administration, monitoring, and follow up improved. This highlights the role of multidisciplinary experience in supporting broader adoption.

Participants also noted early signs of improvement in access and payer alignment. While challenges remain, some clinicians reported fewer denials and more streamlined approval processes over time, particularly as guideline inclusion and clinical familiarity have increased. Participants also highlighted that ropeginterferon alfa-2b aligns with the NCODA Oncology Optimized Limited Distribution (OOLD) model, a distribution approach designed to support medically integrated, patient-centered oncology care by prioritizing dispensing through medically integrated pharmacies and reducing reliance on PBM-affiliated mail-order pharmacies.[9] Clinicians noted that this model helps facilitate more coordinated care, improve communication across the care team, and support more timely treatment initiation.

These changes contribute to a more favorable environment for adoption and may reduce some of the friction previously associated with initiation. As access processes continue to evolve, they are expected to further support integration into routine practice.

Conclusion and Future Directions

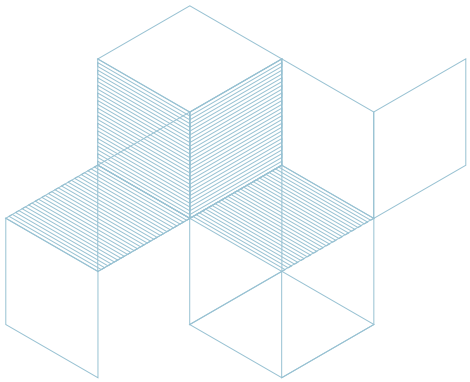
The treatment landscape for PV continues to evolve as clinicians increasingly balance immediate hematologic control with broader goals related to long term disease management, patient experience, and durability of response. Within this shifting paradigm, ropeginterferon alfa-2b is emerging as an important therapeutic option that is reshaping how clinicians think about treatment selection and timing.

Findings from this analysis suggest that adoption is influenced less by questions of clinical value and more by the realities of implementation within everyday oncology practice. Variability across care settings reflects differences in infrastructure, workflow integration, and operational capacity rather than resistance to interferon based therapy itself. At the same time, growing clinical familiarity and multidisciplinary experience are contributing to increased comfort with earlier and more proactive use.

Importantly, many of the challenges identified by participants are addressable through practical strategies already familiar within oncology care delivery. Medically integrated pharmacy support, standardized education, proactive follow up, and coordinated team based care were consistently associated with more efficient implementation and improved patient experience. These findings highlight meaningful opportunities to reduce variability and support broader integration into routine practice.

As clinical evidence continues to expand and operational models mature, the role of ropeginterferon alfa-2b in PV management will likely continue to evolve. Future progress will depend not only on continued research and guideline development, but also on the ability to translate clinical intent into sustainable real world implementation.

Ultimately, the conversation in PV management is moving beyond whether interferon-based therapy should be considered and toward how it can be incorporated most effectively to support individualized, patient-centered care. By aligning clinical goals with practical care delivery strategies, oncology practices have an opportunity to further optimize treatment approaches and improve outcomes for patients living with PV.



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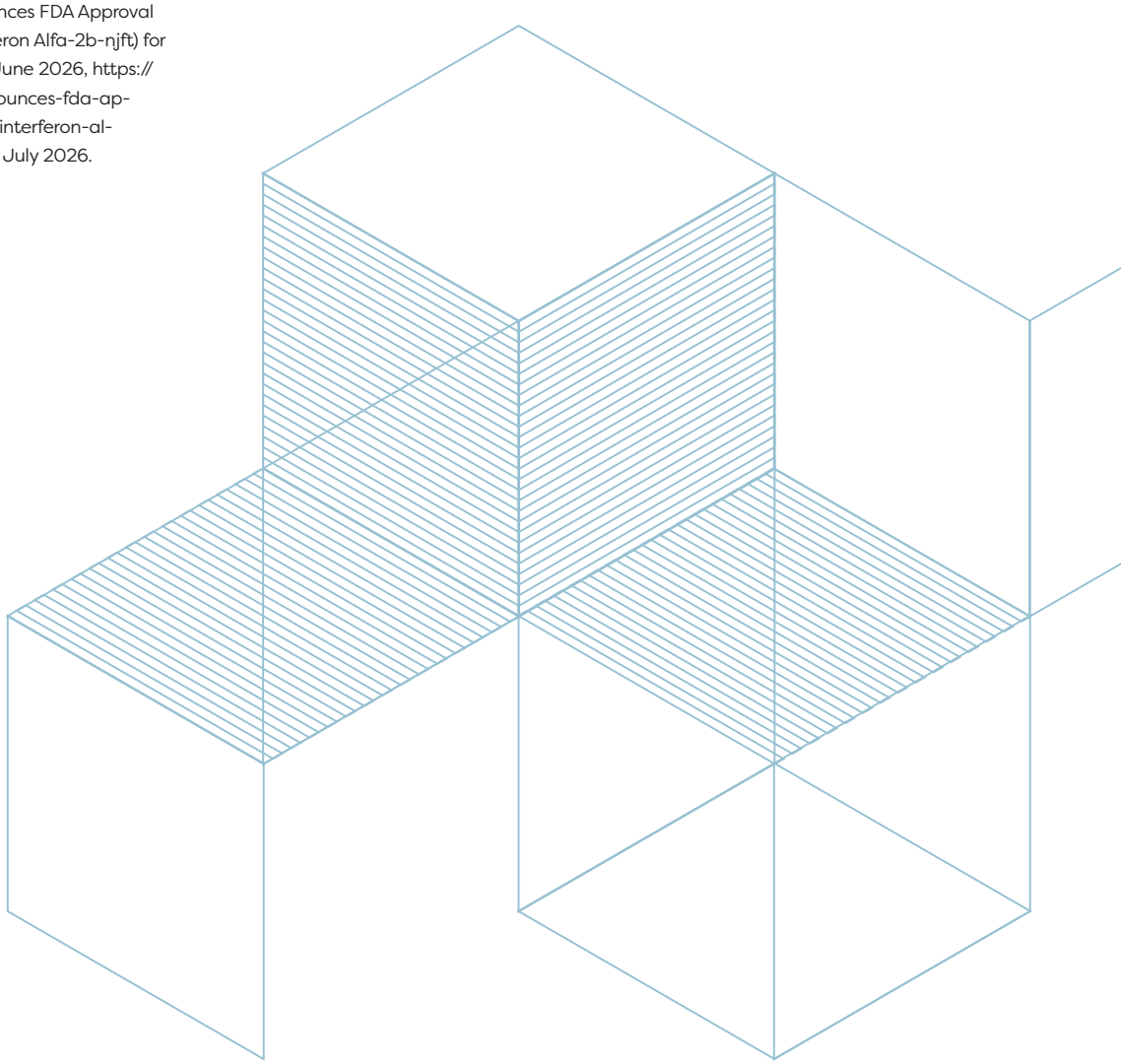

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