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Emicizumab in the Treatment of Hemophilia A. Characteristics and clinical application

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Abstract

Introduction: Hemophilia A is an inherited bleeding disorder caused by a congenital deficiency of factor VIII. It is characterized by a tendency for prolonged and excessive bleeding, both spontaneous and trauma-induced. The treatment of hemophilia A involves the

use of factor VIII replacement therapy. In recent years, emicizumab-a modern, bispecific monoclonal antibody- has gained significant attention as an alternative to traditional treatment methods.

Materials and methods : A total of 30 articles were analyzed, sourced from publicly available databases such as PubMed and Google Scholar. The selection focused on publications addressing molecular structure, pharmacokinetics, and treatment efficacy. The majority of the cited sources were published in English.

State of knowledge: In this article, we will discuss the mechanism of action of emicizumab, its pharmacokinetics, and the benefits of its use in the treatment of hemophilia A, including a comparison with traditional therapies. The results of clinical trials will also be presented, confirming its efficacy, safety, and patient satisfaction, including in the context of treating patients with FVIII inhibitors.The goal is to present the effectiveness, safety, mechanism of action, and pharmacokinetic profile of emicizumab in bleeding prophylaxis for patients with hemophilia A.

Conclusions: Emicizumab is a groundbreaking prophylactic treatment for hemophilia A, effective both in patients with and without factor VIII inhibitors, by mimicking the function of factor VIIIa. Clinical trials HAVEN 1–4 demonstrated the drug's high efficacy in reducing bleeds and significantly lowering annual bleeding rates. Emicizumab has a favorable pharmacokinetic profile, allowing for infrequent dosing and improving therapy comfort compared to traditional treatment.

Key words: Hemophilia A; emicizumab; factor VIII; HAVEN trials; ABR; pharmacokinetics.

Introduction

Hemophilia A is a hereditary bleeding disorder characterized by a deficiency or a substantial reduction in the activity of factor VIII within the coagulation cascade, resulting in compromised hemostasis and a propensity for prolonged hemorrhage. This condition predominantly affects males, while females typically serve as carriers of the genetic mutation. In Poland, the prevalence of hemophilia A is approximately 7 cases per 100,000 individuals. The gene responsible for the synthesis of factor VIII resides on the long arm of the X chromosome. The most prevalent defect associated with the severe manifestation of

hemophilia A is a significant inversion and translocation of exons 1–22, which accounts for roughly 45% of cases. Additional anomalies include point mutations, as well as both large and small deletions. Consequently, these genetic alterations can lead to a complete inhibition of factor VIII production, a marked reduction in its levels, or the synthesis of a dysfunctional protein. In most women who are carriers, factor VIII activity is near the lower limit of normal. Hemophilia may also occur in women due to abnormalities of the X chromosome, such as its inactivation or mutations, or when a woman inherits the hemophilia gene from both parents. It is believed that bleeding in hemophilia results from impaired activity of the intrinsic tenase complex, in which activated factor VIII acts as a cofactor. Disruption of the activity of this complex leads to abnormalities in the blood clotting process, resulting in a tendency toward excessive bleeding. Treatment of hemophilia A involves administering preparations that replace the missing factor VIII. Standard therapy, which uses recombinant factor VIII (rFVIII), however, has its limitations, such as the need for frequent administration and the risk of developing inhibitors. In recent years, emicizumab, a bispecific monoclonal antibody, has gained increasing popularity as a modern alternative in the treatment of hemophilia A [1].

Aim of the Study

The aim of this work is to provide a detailed analysis of the properties of emicizumab, a modern drug used in the prophylaxis of hemophilia A, including its chemical structure, mechanism of action, pharmacokinetics, and clinical efficacy. The study aims to compare the effectiveness and safety of emicizumab therapy with traditional treatment using recombinant factor VIII, with particular emphasis on its impact on bleeding frequency, patient quality of life, and the potential therapeutic benefits resulting from subcutaneous administration. In addition, the objective is to assess the role of emicizumab in the modern approach to the treatment of hemophilia A and its significance in improving the comfort and life expectancy of affected individuals.

Review Methods

The study employed a literature review method focusing on scientific publications concerning emicizumab and its use in the treatment of hemophilia A. Source materials were searched in medical databases such as PubMed, Scopus, and Google Scholar, including publications in both Polish and English. The criteria for selecting articles included their

relevance, scientific reliability, and relation to the topics of emicizumab's structure, mechanism of action, pharmacokinetics, and clinical efficacy. The analysis encompassed clinical studies, systematic reviews, and expert guidelines. The collected information was subjected to critical evaluation and synthesis to present a comprehensive overview of the application of emicizumab in clinical practice.

State of knowledge

The unique structure of emicizumab results from its bispecific nature—meaning that it possesses two different antigen-binding sites. One arm of the antibody is designed to bind activated factor IX (FIXa), while the other binds factor X (FX) [2,3]. Emicizumab mimics the function of factor VIII (FVIII). In the physiological coagulation cascade, activated factor VIII (FVIIIa) acts as a cofactor by bringing FIXa and FX into proximity, enabling FIXa to activate FX. Thanks to its bispecific structure, emicizumab plays a similar "bridging" role, linking FIXa and FX and allowing the activation of factor X even in the absence or deficiency of functional factor VIII [2,4,5]. Emicizumab is also a modified IgG4-class immunoglobulin. While it is based on a human IgG4 framework, modifications were introduced in the Fc region to limit potential interactions with other components of the immune system (effector functions) and to prolong the drug's half-life in the body [2,5–7].

The key structural features of the emicizumab molecule are as follows:

1. Bispecificity – unlike standard antibodies, which have two identical antigen-binding sites, emicizumab possesses two different binding sites. One arm of the antibody binds activated factor IX (FIXa), and the other binds factor X (FX) [2].
2. Humanization and IgG4 type – the molecule has been "humanized," meaning its structure was modified to resemble human antibodies as closely as possible (in this case immunoglobulin G4), which reduces the risk of an immune response [8]. It is a monoclonal antibody, meaning all its molecules are identical [9].
3. Lack of homology with factor VIII – emicizumab does not exhibit structural similarity or amino acid sequence homology with factor VIII (FVIII). It acts by mimicking the function of the missing or nonfunctional activated factor VIII (FVIIIa) in the coagulation cascade [8,10,11].

4. Mechanism of action related to its structure – due to its bispecific structure, emicizumab functions as a molecular "bridge" simultaneously binding FIXa (the enzyme) and FX (the substrate) on a phospholipid surface (e.g., activated platelets), thereby enabling FX activation by FIXa even in the absence of FVIIIa [7,12].
5. Production technology – emicizumab is produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells [13].
6. Molecular weight – the approximate molecular weight of emicizumab is 145.6 kDa [13].

Pharmacokinetics

The pharmacokinetics of emicizumab include several key aspects that influence its effectiveness and use in the treatment of hemophilia. After subcutaneous administration, emicizumab is characterized by efficient absorption. As a monoclonal antibody, it demonstrates high bioavailability when administered subcutaneously. The maximum plasma concentration (Cmax) is reached within 1 to 3 days after administration [14]. The drug's absorption is dose-independent, meaning its bioavailability does not change with the amount administered [11,15].

Following subcutaneous injection, emicizumab exhibits wide distribution throughout the body, although it does not readily cross the blood–brain barrier. As a monoclonal antibody, it binds to plasma proteins and circulating cells, and its distribution is primarily limited to the intravascular and interstitial spaces [16]. The drug distributes mainly within body fluids, including plasma, and in tissues where coagulation processes occur.

Emicizumab does not undergo classical hepatic metabolism typical of many other drugs. As a monoclonal antibody, it is metabolized mainly through the reticuloendothelial system (RES), which includes cells in the liver, spleen, and bone marrow [8,11]. Within these organs, which are rich in macrophages, phagocytosis, degradation, and clearance of antibodies take place. Monoclonal antibodies such as emicizumab are broken down through proteolytic processes, in which proteolytic enzymes digest the molecule into smaller fragments that are subsequently eliminated from the body. This process is slower than the metabolism of synthetic drugs, contributing to the longer half-life of emicizumab.

As a result, emicizumab provides prolonged activity, allowing dosing every few weeks—unlike other hemophilia therapies, which require more frequent administration. It is also worth noting that because the RES is responsible for eliminating foreign proteins such as monoclonal antibodies, emicizumab does not rely on hepatic enzymes. This minimizes the risk of drug–drug interactions and makes emicizumab therapy safer and less susceptible to typical pharmacokinetic interactions seen with drugs metabolized in the liver [14,18].

The half-life of emicizumab ranges from 30 to 40 days [17]. This relatively long half-life means the drug remains in the body for an extended period once administered. Consequently, patients using emicizumab can receive it at longer intervals—most commonly once weekly, or even every few weeks, depending on the treatment regimen [8,11].

Effectiveness of Emicizumab

The effectiveness of emicizumab has been confirmed in several randomized phase III clinical trials (including HAVEN 1, HAVEN 2, HAVEN 3, and HAVEN 4), as well as in numerous observational analyses based on real-world clinical practice data. Key parameters used to assess the drug's efficacy include: the number of bleeding episodes requiring medical intervention, improvements in health-related quality of life, reductions in the need for other coagulation factors, and the overall safety profile of the therapy.

The HAVEN 1 study evaluated the effectiveness of emicizumab in adults and adolescents with hemophilia A and with inhibitors to factor VIII. Participants were divided into two groups: one received prophylactic emicizumab at a dose of 1.5 mg/kg once weekly, and the control group was treated on demand with bypassing agents (e.g., activated prothrombin complex concentrate [aPCC] or recombinant activated factor VII [rFVIIa]). In the emicizumab group, the median annualized bleeding rate (ABR) was 2.9, compared with 23.3 in the control group—corresponding to an approximately 87% reduction in treated bleeding episodes. Importantly, 63% of patients receiving emicizumab experienced no bleeding episodes requiring treatment during the study [11].

The HAVEN 2 study focused on pediatric patients with hemophilia A and factor VIII inhibitors. Emicizumab demonstrated high effectiveness in this population: 77% of participants experienced no treated bleeding episodes during the observation period, and the

median ABR was 0.3 [18]. Caregivers reported a clear improvement in the children's quality of life and a significant reduction in psychological burden associated with frequent intravenous infusions.

The HAVEN 3 study assessed the effectiveness of emicizumab in patients with hemophilia A without inhibitors. Prophylactic regimens (1.5 mg/kg weekly or 3 mg/kg every two weeks) resulted in a marked reduction in ABR compared with on-demand treatment. Median ABR values were 1.5 and 1.3 in the weekly and biweekly dosing groups, respectively, compared with 38.2 in the group without prophylaxis [8]. Additionally, 55% of those receiving prophylactic emicizumab experienced no bleeding episodes requiring treatment.

The HAVEN 4 study evaluated the effectiveness of once-monthly administration of emicizumab (6 mg/kg) in patients with hemophilia A, both with and without inhibitors. In this cohort, 56% of patients experienced no bleeding episodes, and the median ABR was 0, confirming the high efficacy of the drug even with extended dosing intervals [19].

Emicizumab demonstrates its therapeutic value not only in controlled clinical trial settings but also in everyday clinical practice, further solidifying its credibility as an effective prophylactic agent. Its use leads to significant clinical improvement in patients with severe hemophilia A, as reflected in the reduction of annualized bleeding rates (ABR) and the increased proportion of patients who remain bleed-free after transitioning from factor VIII–based therapy to emicizumab prophylaxis [20].

Table 1: Comparison of HAVEN 1–4 Studies on Emicizumab

Study	Population	FVIII inhibitors	Emicizumab dosing regimen	ABR (emicizumab)	% of patients with no bleeding	Comparator group
HAVEN 1	Adults and adolescents ≥12 y	Yes	1.5 mg/kg once weekly	2.9	63%	On-demand treatment (aPCC, rFVIIa)

HAVEN 2	Children <12 y	Yes	1.5 mg/kg once weekly	0.3	77%	No comparator group (open-label)
HAVEN 3	Adults and adolescents ≥12 y	No	1.5 mg/kg once weekly or 3 mg/kg every 2 weeks	1.5	55–56%	FVIII prophylaxis or on-demand treatment
HAVEN 4	Adults ≥18 y	Yes or No	6 mg/kg once monthly	2.4 (median ABR = 0)	56%	No comparator group (open-label design)

Emicizumab vs. rFVIII Replacement Therapy

Emicizumab is characterized by a low annualized bleeding rate (ABR) compared to replacement therapy with standard or extended half-life recombinant factor VIII (rFVIII). In the HAVEN 1–4 studies, the calculated mean ABR for treated bleeding episodes generally decreased over consecutive 24-week treatment periods. The median ABR for treated bleeds remained at 0 throughout the study period. In the final study period (weeks 121–144), 97.6% of patients treated with emicizumab reported ≤3 treated bleeding episodes, and 82.4% experienced no bleeds requiring intervention.

The effectiveness of emicizumab in reducing ABR was similar in patients both with and without factor VIII inhibitors. Across all studies, the proportion of participants who experienced no spontaneous bleeds remained above 91%. In the last 24-week period, 90.0% of patients had no bleeds in the joints requiring treatment. Throughout HAVEN 1–4, the modeled ABR for all bleeds was 2.6 (95% CI: 2.2–3.1). The mean ABR for all bleeds—including untreated bleeds and those treated with clotting factor concentrates—decreased with

each 24-week treatment period. The median ABR for all bleeds was 0 in each analyzed period. The proportion of participants experiencing no bleeds increased with each study phase. Between weeks 121 and 144, 74.1% of participants had no bleeding, and 97.6% reported ≤3 bleeds. The median number of bleeds in the 24 weeks before study entry was 8.0 (IQR: 5.0–15.0) [21].

According to HAVEN 1–4, the half-life of emicizumab is approximately 30 days [22], which is advantageous compared to rFVIII with a standard half-life (8–12 hours) or extended half-life (mean 18.8 hours) [23]. The emicizumab dosing regimen was initially developed based on pharmacokinetic and population efficacy models, aiming to rapidly achieve and maintain therapeutic drug levels [24]. Thanks to its long half-life, emicizumab can be administered as follows: 1.5 mg/kg weekly, 3 mg/kg every two weeks, or 6 mg/kg every four weeks.

In studies, consistent with pharmacokinetic modeling, average trough concentrations of emicizumab >50 µg/mL were achieved by the end of the loading dose phase in HAVEN 1–4 and maintained throughout the observation period (up to 3.5 years). These levels provided sustained therapeutic effect for most participants [25].

Emicizumab is administered subcutaneously, which is more patient-friendly. Less frequent dosing and a less invasive route of administration improve adherence. Subcutaneous injections are particularly important in prophylaxis for children with hemophilia A, for whom intravenous access can be traumatic, and in older adults, where intravenous access is challenging. Subcutaneous administration also allows for stable drug concentrations over longer periods [26]. The procedure does not require medical personnel and can be performed at home.

In the HAVEN 3 study, a patient satisfaction analysis compared intravenous rFVIII prophylaxis with subcutaneous emicizumab. Sixty-three participants who previously received rFVIII prophylaxis were switched to emicizumab. They completed the 15-point Subcutaneous/Intravenous Hemophilia Injection Satisfaction Questionnaire (SQ-ISHI), rating satisfaction from 0 (“not at all satisfied”) to 10 (“completely satisfied”). Before emicizumab, mean overall satisfaction with rFVIII prophylaxis was 6.9 (95% CI: 6.2–7.7). After 21/25 weeks of emicizumab therapy, participants reported less difficulty, lower impact on daily life,

fewer worries and burdens, greater confidence, and higher overall satisfaction. Mean overall satisfaction increased to 8.8 (95% CI: 8.4–9.3).

The highest proportion of patients reported significant improvements (≥2 points) in treatment impact on travel (50%), time burden (48%), inconvenience, and satisfaction with "life spontaneity" (46%). Fifty-five out of 60 respondents (92%) indicated they were "much more" or "far more" satisfied with hemophilia treatment. No participant reported decreased satisfaction; only 2 individuals (3%) noted no change. These SQ-ISHI results demonstrate that patients treated with emicizumab were more satisfied across all assessed areas than during prior intravenous rFVIII prophylaxis [27].

Development of anti-emicizumab antibodies is rare. Binding antibodies developed in 5% of patients, but only >1% resulted in neutralization, leading to prophylaxis failure. This is a substantial improvement compared to rFVIII, where up to 30% of patients may develop inhibitors, a major clinical concern [16,22].

Due to its mechanism of action, emicizumab is first-line therapy for bleeding prophylaxis in patients with hemophilia A and factor VIII inhibitors. HAVEN 1–4 studies showed comparable efficacy regardless of inhibitor status, making the drug suitable for adults and children [21].

Emicizumab should not be used for acute bleeds, as concomitant administration of aPCC (activated prothrombin complex concentrate) increases thrombotic risk. This risk has not been observed with combined rFVIII and aPCC treatment [26,28]. In the initial HAVEN 1 study, five patients with inhibitors experienced thrombotic events (TE), including three cases of thrombotic microangiopathy (TMA) when acute bleeds were treated with high cumulative doses of aPCC (>100 U/kg/24h) for ≥24 hours. TMA resolved after discontinuing aPCC. Additionally, 37 thrombotic events unrelated to aPCC were reported, mostly associated with ≥1 cardiovascular risk factor (e.g., myocardial infarction, coronary disease, hypertension, hypercholesterolemia, smoking, advanced age) or other prothrombotic conditions (e.g., sepsis, infection, trauma, hepatitis C). Seventeen events (45.9%) occurred in patients with FVIII inhibitors.

During a two-year follow-up, no new thrombotic or TMA events occurred after implementing aPCC restrictions [29]. In total, four thrombotic events were fatal: two myocardial infarctions in patients with multiple comorbidities and two cases of disseminated intravascular coagulation (DIC) in patients >70 years old with pneumonia. Of events with reported outcomes, 20 of 31 (64.5%) were fully resolved or improving at the time of analysis [30]. In most cases, prophylactic emicizumab was not interrupted due to thrombotic events. Overall, the benefit-risk profile of emicizumab remained favorable and unchanged after the study.

Conclusions

Emicizumab represents a breakthrough in prophylactic treatment of hemophilia A, both in patients with and without factor VIII inhibitors. Its unique mechanism, based on a bispecific antibody structure, effectively mimics the function of factor VIIIa, providing bleed control independent of inhibitor presence. Data from the HAVEN 1–4 clinical trials clearly demonstrate the high efficacy of emicizumab in reducing bleeding episodes, reflected in significantly lower annualized bleeding rates (ABR). A high proportion of patients—over 80%—experienced no bleeding episodes, highlighting the drug's exceptional long-term prophylactic effectiveness.

Emicizumab also exhibits a favorable pharmacokinetic profile, with high bioavailability after subcutaneous administration and a long half-life (30–40 days), enabling infrequent dosing (weekly, every two weeks, or every four weeks). Patient-reported outcomes confirm a substantial improvement in treatment convenience and satisfaction compared to previous intravenous rFVIII prophylaxis.

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References:

1. Szczeklik A. Gajewski P. Interna Szczeklika 2024. Medycyna Praktyczna, Kraków 2024.

2. Lenting PJ, Denis V, Christophe OD. Perspective Emicizumab, a bispecific antibody recognizing coagulation factors IX and X: how does it actually compare to factor VIII? Blood. 2017; Vol. 130: 2463-67. https://doi.org/10.1182/blood-2017-08-801662

3. Yada K, Nogami K. Novel Insights and New Developments Regarding Coagulation Revealed by Studies of the Anti-Factor IXa (Activated Factor IX)/Factor X Bispecific Antibody, Emicizumab. Arteriosclerosis, Thrombosis, and Vascular Biology. Lippincott Williams and Wilkins; 2020; Vol. 40:1148–54. https://doi.org/10.1161/ATVBAHA.120.312919

4. Summary of product characteristics https://ec.europa.eu/health/documents/community register/2018/20180223140159/anx_140159_en.pdf

5. Yoneyama K, Schmitt C, Portron A, Kiialainen A, Kotani N, Jaminion F, et al. Clinical pharmacology of emicizumab for the treatment of hemophilia A. Expert Review of Clinical Pharmacology. Taylor and Francis Ltd. 2023; Vol. 16: 775–90. https://doi.org/10.1080/17512433.2023.2243213

6. Voorberg J, Postmus T, Schols S. Next generation FVIII mimetic bispecific antibody for hemophilia A. Journal of Thrombosis and Haemostasis. John Wiley and Sons Inc. 2022;Vol. 20:1301–5. https://doi.org/10.1111/jth.15705

7. Sampei Z, Igawa T, Soeda T, et al. Identification and multidimensional optimization of an asymmetric bispecific IgG antibody mimicking the function of factor VIII cofactor activity. PLoS One. 2013; 8(2):57479. https://doi.org/10.1371/journal.pone.0057479

8. Oldenburg J, Mahlangu JN, Kim B, Schmitt C, Callaghan MU, Young G, et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors. New England Journal of Medicine. 2017 Aug 31; 377(9):809–18. https://doi.org/10.1371/journal.pone.0057479

9. Scott LJ, Kim ES. Emicizumab-kxwh: First Global Approval. Drugs. https://pubmed.ncbi.nlm.nih.gov/29357074/

10. Gelbenegger G, Schoergenhofer C, Knoebl P, Jilma B. Bridging the Missing Link with Emicizumab: A Bispecific Antibody for Treatment of Hemophilia A. Thromb Haemost. 2020 Oct 1; 120(10):1357–70. https://doi.org/10.1055/s-0040-1714279

11. Mahlangu J, Oldenburg J, Paz-Priel I, Negrier C, Niggli M, Mancuso ME, et al. Emicizumab Prophylaxis in Patients Who Have Hemophilia A without Inhibitors. New England Journal of Medicine. 2018 Aug 30; 379(9):811–22. https://doi.org/10.1056/nejmoa1803550

12. Lillicrap D, Fijnvandraat K, Young G, Mancuso ME. Patients with hemophilia A and inhibitors: prevention and evolving treatment paradigms. Expert Rev Hematol. https://www.tandfonline.com/doi/abs/10.1080/17474086.2020.1739518

13. Starting Hemlibra Quick Reference Guide https://www.hemlibra-hcp.com/dosing-and administration/dosing.html (dostęp: 2025.05.10).

14. Schmitt C, Adamkewicz JI, Xu J, Petry C, Catalani O, Young G, et al. Pharmacokinetics and Pharmacodynamics of Emicizumab in Persons with Hemophilia A with Factor VIII Inhibitors: HAVEN 1 Study. Thromb Haemost. 2021 Mar 1;121(3):351–60. https://doi.org/10.1055/s-0040-1717114

15. Kotani N, Yoneyama K, Kawakami N, Shimuta T, Fukase H, Kawanishi T. Relative and Absolute Bioavailability Study of Emicizumab to Bridge Drug Products and Subcutaneous

Injection Sites in Healthy Volunteers. Clin Pharmacol Drug Dev. 2019 Aug 1;8(6):702–12. https://doi.org/10.1002/cpdd.617

16. Windyga J. Emicizumab in severe hemophilia A. Acta Haematol Pol. https://journals.viamedica.pl/acta_haematologica_polonica/article/view/AHP.2021.0079

17. Nogami K. Bispecific antibody mimicking factor VIII. Thromb Res. https://www.thrombosisresearch.com/action/showFullText?pii=S0049384816303619

18. Young G, Liesner R, Chang T, Sidonio R, Oldenburg J, Jiménez-Yuste V, et al. A multicenter, open-label phase 3 study of emicizumab prophylaxis in children with hemophilia A with inhibitors. Blood. https://pmc.ncbi.nlm.nih.gov/articles/PMC6908828/

19. Pipe SW, Shima M, Lehle M, Shapiro A, Chebon S, Fukutake K, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. Lancet Haematol. https://www.thelancet.com/action/showFullText?pii=S2352302619300547

20. Escuriola Ettingshausen C, Eberl W, Eichler H, Fischer R, Hart C, Holstein K, et al. Efficacy of emicizumab in patients with severe haemophilia A without factor VIII inhibitors in Germany: evaluation of real-life data documented by the smart medication eDiary. Ther Adv Hematol. 2024 Jan 1;15. https://doi.org/10.1177/20406207241295653

21. Callaghan MU, Negrier C, Paz-Priel I, Chang T, Chebon S, Lehle M, et al. Long-term outcomes with emicizumab prophylaxis for hemophilia A with or without FVIII inhibitors from the HAVEN 1-4 studies. http://ashpublications.org/blood/article-pdf/137/16/2231/1805347/bloodbld2020009217.pdf

22. Powell JS, Josephson NC, Quon D, Ragni M V, Cheng G, Li E, et al. Safety and prolonged activity of recombinant factor VIII Fc fusion protein in hemophilia A patients Current factor VIII (FVIII) products display a half-life (t 1/2) of 8-12 hours, requiring frequent intravenous injections for pro-phylaxis and treatment of patients with hemophilia. http://ashpublications.org/blood/article pdf/119/13/3031/1348603/zh801312003031.pdf

23. Yoneyama K, Schmitt C, Kotani N, Levy GG, Kasai R, Iida S, et al. A Pharmacometric Approach to Substitute for a Conventional Dose-Finding Study in Rare Diseases: Example of Phase III Dose Selection for Emicizumab in Hemophilia A. Clin Pharmacokinet. 2018 Sep 1;57(9):1123–34. https://doi.org/10.1007/s40262-017-0616-3

24. Kiialainen A, Adamkewicz JI, Petry C, Oldenburg J, Pipe SW, Young G, et al. Pharmacokinetics and coagulation biomarkers in children and adults with hemophilia A receiving emicizumab prophylaxis every 1, 2, or 4 weeks. Res Pract Thromb Haemost. 2024 Jan 1;8(1). https://doi.org/10.1016/j.rpth.2023.102306

25. Franchini M, Mannucci PM. The More Recent History of Hemophilia Treatment. Semin Thromb Hemost. 2022 Nov 1;48(8):904–10. https://doi.org/10.1055/s-0042-1756188

26. Kempton C, Trask P, Parnes A, Niggli M, Campinha-Bacote A, U. Callaghan M, et al. Development and testing of the Satisfaction Questionnaire with Intravenous or Subcutaneous Hemophilia Injection and results from the Phase 3 HAVEN 3 study of emicizumab prophylaxis in persons with haemophilia A without FVIII inhibitors. Haemophilia. 2021 Mar 1;27(2):221–8. https://doi.org/10.1111/hae.14222

27. Mannucci PM. Hemophilia treatment innovation: 50 years of progress and more to come. Journal of Thrombosis and Haemostasis. Elsevier B.V. 2023; Vol. 21: p. 403–12. https://doi.org/10.1016/j.jtha.2022.12.029

28. Lewandowska M, Nasr S, Shapiro AD. Emerging Therapies in Hemophilia: Improving Equitable Access to Care. Journal of Blood Medicine. Dove Medical Press Ltd. 2025; Vol.16:95–115. https://doi.org/10.2147/jbm.s490588

29. Parnes A. In hemophilia, it just keeps getting better. Blood. Elsevier B.V. 2021; Vol. 137:2135–6. https://doi.org/10.1182/blood.2020010238

30. Howard M, McKinley D, Sanabria F, Ko R, Nissen F. Evaluation of the Safety of Emicizumab Prophylaxis in Persons with Hemophilia A: An Updated Summary of Thrombotic Events and Thrombotic Microangiopathies. Blood. 2021 Nov 5;138:3186. https://doi.org/10.1182/blood-2021-146147