Classification: Official-Sensitive

Clinical Priorities Advisory Group Summary Report

Agenda item	2.2
Date of Meeting	07/05/2025
Title of the Proposition	Emicizumab for prophylaxis of bleeding episodes in people with moderate haemophilia A without factor VIII inhibitors (all ages)
Unique Reference Number	2333
Programme of Care	Blood & Infection
Clinical Reference Group	Specialised Blood Disorders
Service/treatment status	delegated

Action requested

Support the adoption of the policy proposition

Recommended its approval as an in year service development.

Summary of the proposition:

Emicizumab is recommended to be made available for prophylaxis of bleeding episodes in people with moderate haemophilia A without factor VIII inhibitors. This is proposed as a routinely commissioned treatment option for all ages, in line with the product licence. The commissioning criteria target treatment only for those with a severe bleeding phenotype

Publication reference: PRNxxx

and therefore not all patients with moderate haemophilia A. This policy proposition represents a small extension to the current use of emicizumab which is now established as the standard of care in prophylaxis of severe haemophilia A.

Clinical Panel recommendation:

The Clinical Panel recommended that the policy proposition progress as a routine commissioning policy.

Assurances

The committee is asked to receive the following assurance:		
1.	The Deputy Director of Clinical Effectiveness confirms the proposition has completed the appropriate sequence of developmental and governance steps.	
2.	The Deputy Director of Acute Programmes confirms the proposition is supported by the following documentation (please tick the box where applicable)	
	Draft Clinical Commissioning policy proposition	☒
	Evidence Review	☒
	Public Health Evidence Report	☐
	Evidence to Decision Making (EtD) Summary	☒
	Equalities and Heath Inequalities Assessment (EHIA)	☒
	Prior Approval Form	☒
	Engagement Report	☒
	13Q Assessment and Patient & Public Voice Assurance	☒
	Clinical Panel Report	☒
	Policy Working Group membership	☒
	Other (please state if required)	☐
3.	The Deputy Director of Finance (Specialised Commissioning) confirms that the Impact Assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.	
4.	The Director of Clinical Commissioning (Specialised Commissioning) confirms that the Service and Operational Impact Assessments have been completed.	

5.	The Deputy Director of Quality and Nursing (Specialised Commissioning) confirms that the proposed quality indicators have been adequately defined (where applicable).

Evidence Review Summary

In people with moderate haemophilia A without inhibitors, what is the clinical effectiveness and safety of emicizumab prophylaxis compared with current standard care?

Outcome	Evidence statement
Clinical Effectiveness	
Critical outcomes	
Rate of treated bleeding events **Certainty of evidence:** Very low	Rate of treated bleeding events is important to patients because bleeding events can cause serious complications including disability and death. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to rate of treated bleeding events (Négrier et al. 2023, n=72) in people with moderate (n=51) or mild haemophilia A (n=21) without FVIII inhibitors, who warranted prophylaxis based on the treating physician's assessment. After a median of 55.6 weeks (interquartile range (IQR) 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors (n=72) the model-based annualised bleed rate (ABR) for treated bleeds was 0·9 (95% confidence interval (CI) 0.55 to 1.52). Model-based ABR accounts for different follow-up times. Baseline ABR for treated bleeds was not provided. **(VERY LOW)** • Négrier et al. 2023 showed that in people with moderate haemophilia A without inhibitors (n=51) the model-based ABR for treated bleeds was 0.9 (95% CI 0.50 to 1.78). Model-based ABR accounts for different follow-up times. Baseline ABR for treated bleeds was not provided. **(VERY LOW)** Treated bleeds were defined as bleeds in which coagulation factors were given to treat signs or symptoms of bleeding. Two bleeds of the same type and at the same anatomical location were considered to be 1 bleed if the second bleed occurred within 72 hours from the last treatment for the first bleed. **This study provides very low certainty evidence for the rate of treated bleeding events in people after a median of 55.6 weeks of emicizumab treatment. In 72 people with mild or moderate haemophilia A without inhibitors, the model-based ABR for treated bleeds was 0.9. In 51 people with moderate haemophilia A without inhibitors, the model-based ABR was also 0.9. However, baseline ABRs for treated bleeds were not provided, so no conclusions can be drawn about the effect of emicizumab on the rate of treated bleeds.**

Rate of all bleeding events **Certainty of evidence:** Very low	Rate of all bleeding events is important to patients because bleeding events can cause serious complications including disability and death. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to rate of all bleeding events (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors (n=72) the model-based ABR for all bleeds was 2.3 (95% CI 1.67 to 3.12) compared with 10.1 (95% CI 6.93 to 14.76) over the 24 weeks before study entry. Model-based ABR accounts for different follow-up times. No statistical analysis reported. **(VERY LOW)** • Négrier et al. 2023 showed that in people with moderate haemophilia A without inhibitors (n=51) the model-based ABR for all bleeds was 2.2 (95% CI 1.57 to 3.20) compared with 6.0 (95% CI 4.33 to 8.22) over the 24 weeks before study entry. Model-based ABR accounts for different follow-up times. No statistical analysis reported. **(VERY LOW)** **This study provides very low certainty evidence that a median of 55.6 weeks of emicizumab treatment reduced the model-based ABR for all bleeds from 10.1 to 2.3 in 72 people with mild or moderate haemophilia A without inhibitors, and from 6.0 to 2.2 in 51 people with moderate haemophilia A without inhibitors. However, no statistical analyses were reported.**
Joint health **Certainty of evidence:** Very low	Joint health is important to patients because joint arthropathy and target joints (when there is recurrent bleeding into a certain joint) occur due to joint bleeding in haemophilia A. This complication is irreversible and causes pain, disability, and difficulty with activities of daily living. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to joint health over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks) (Négrier et al. 2023, n=72). After 52 weeks on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, who had target joints at baseline and were in the study for at least 52 weeks, 20/21 (95%) had resolved joints. Resolved joints were defined in the study as a report of fewer than three bleeds over a 52-week period. **(VERY LOW)** Target joints were defined as joints with 3 or more bleeds occurring in the same joint during the last 24 weeks or unresolved target joints, defined as a target joint that does not fulfil the criterion of 2 or less bleeds into this joint within a consecutive 12-month period. At week 49 on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, mean total Haemophilia Joint Health Score (HJHS) was 6.48 (standard deviation (SD) 8.96) in 56 participants. This compared with 7.20 (SD 10.37) in 65 participants at baseline, with a mean change from baseline of −1.25 (SD 3.95) in 52 participants. **(VERY LOW)** The HJHS measures joint health of the joints most commonly affected by bleeding in haemophilia: the knees, ankles, and elbows. The maximum total

	score is 124. Higher scores indicate worse joint health. Due to irreversible joint damage expected in adults, large improvements in HJHS score in adults over the timeframe of the study would not be expected. **This study provides very low certainty evidence that emicizumab resolved target joints in 20/21 (95%) people with mild or moderate haemophilia A without inhibitors, who had target joints at baseline and were in the study for at least 52 weeks. Data for people with moderate severity haemophilia A were not reported separately.** **This study provides very low certainty evidence that 49 weeks of emicizumab treatment improved the mean total HJHS in 72 people with mild or moderate haemophilia A without inhibitors compared with baseline. The clinical significance of the improvement is unclear. Data for people with moderate haemophilia A were not reported separately.**
Important outcomes	
Health related quality of life (HRQL) **Certainty of evidence:** Very Low	Health related quality of life is important to patients because it provides a holistic evaluation and indication of the patient's general health and their perceived well-being and their ability to participate in activities of daily living. This outcome is both a key indicator of the effectiveness of treatment and provides an insight into the patient's perception of the effectiveness of treatment. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to health related quality of life over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks) (Négrier et al. 2023, n=72). At week 49 and week 61 on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, the CATCH mean scores in the treatment burden domain were reported to show a trend to improvement in children, young people and adults aged 8 years or older (n=60). However, the results were only presented graphically (up-to week 61), and interpretation is difficult. Other domains were reported to be stable, with baseline values maintained until week 49. Specific values for these outcomes were not reported. **(VERY LOW)** The CATCH (the Comprehensive Assessment Tool of Challenges in Haemophilia) is a tool to assess outcomes important to children, young people, and adults with haemophilia. It includes domains related to quality of life, lifestyle restrictions, physical activity, and treatment burden. In adults irreversible joint damage may contribute to quality of life assessment scores and large improvements for this age group over the timeframe of the study would not be expected. **This study provides very low certainty evidence that there is a trend to improvement in treatment burden with up-to 61 weeks of emicizumab treatment, as measured by the CATCH assessment tool in 60 people aged 8 years and over with mild or moderate haemophilia A without inhibitors. All other domains of the CATCH assessment tool remained stable at week 49. The clinical significance of this is unclear. Data for people with moderate haemophilia A were not reported separately.**
Patient treatment preference **Certainty of evidence:** Very low	Patient treatment preference is important to patients as it reflects the burden of treatment and is a surrogate marker for control of symptoms and quality of life, and safety/adverse events. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to patient treatment preference over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks) (Négrier et al. 2023, n=72). At week 17 on emicizumab treatment: • Négrier et al. 2023 showed that in young people and adults aged 12 years or older with mild or moderate haemophilia A without inhibitors

	responding to the EmiPref questionnaire, 50/52 (96%) preferred emicizumab to their previous treatment. **(VERY LOW)** • Négrier et al. 2023 showed that in caregivers responding to the EmiPref questionnaire, 24/28 (86%) preferred emicizumab to their child's previous treatment. **(VERY LOW)** The EmiPref Questionnaire is a questionnaire to assess treatment preference. Participants or caregivers were asked to report what treatment regimen they preferred: emicizumab or their pre-study treatment. The questionnaire was conducted at week 17 in the study. **This study provides very low certainty evidence that the majority of people with mild or moderate haemophilia A without inhibitors aged 12 years and over (96%), and caregivers (86%), preferred emicizumab to their, or their child's, previous treatment, when responding to the EmiPref questionnaire after 17 weeks of treatment. Data for people with moderate haemophilia A were not reported separately.**
Rate of joint bleeding events **Certainty of evidence:** Very low	Rate of joint bleeding events is important to patients because joint arthropathy secondary to haemophilia A is an irreversible complication that causes pain and difficulty with activities of daily living. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to rate of joint bleeding events (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors (n=72) the model-based ABR for treated joint bleeds was 0.2 (95% CI 0.09 to 0.57). Model-based ABR accounts for different follow-up times. Baseline ABR for treated joint bleeds was not provided. **(VERY LOW)** • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors and target joints at baseline (n=24) the model-based ABR for treated target joint bleeds was 0.1 (95% CI 0.03 to 0.40). Model-based ABR accounts for different follow-up times. Baseline ABR for treated target joint bleeds was not provided. **(VERY LOW)** **This study provides very low certainty evidence for the rate of treated joint bleeds in people after a median of 55.6 weeks of emicizumab treatment. In 72 people with mild or moderate haemophilia A without inhibitors, the model-based ABR for treated joint bleeds was 0.2. In 24 people with mild or moderate haemophilia A without inhibitors and target joints at baseline, the model-based ABR for treated target joint bleeds was 0.1. However, baseline ABRs were not provided, so no conclusions can be drawn about the effect of emicizumab on the rate of treated joint bleeds. Data for people with moderate haemophilia A were not reported separately.**
Activities of daily living **Certainty of evidence:** Very low	Activities of daily living is important to patients because it reflects daily functioning and how well people can engage in education, employment, and recreational activities. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to activities of daily living over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks) (Négrier et al. 2023, n=72). At week 49 on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, aged 5 years or older, duration of time spent in moderate-to-vigorous activity and mean daily step count were reported to be stable from baseline to week 49 (n=not reported). Specific

	values for these outcomes were not reported. The results were presented graphically. **(VERY LOW)** **This study provides very low certainty evidence that duration of time spent in moderate-to-vigorous activity and mean daily step count remained stable in people aged 5 years and over with mild or moderate haemophilia A without inhibitors after 49 weeks of emicizumab treatment compared with baseline. Data for people with moderate haemophilia A were not reported separately.**
Safety	
All adverse events **Certainty of evidence:** Very low	Safety is important to patients as it reflects the risks involved in what is likely to be a long-term prophylactic treatment. This allows a risk benefit assessment to be undertaken. One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, 60/72 (83%) had an adverse event. The most common adverse events were headache (12/72, 17%), injection-site reaction (12/72, 17%) and arthralgia (11/72, 15%). **(VERY LOW)** • Négrier et al. 2023 showed that in people with moderate haemophilia A without inhibitors, 42/51 (82%) had an adverse event. Injection-site reactions were reported by 8/51 (16%). **(VERY LOW)** **This study provides very low certainty evidence that the most commonly reported adverse events with emicizumab were headache, injection-site reactions and arthralgia, reported in 15 to 17% of people with mild to moderate haemophilia A without inhibitors. A similar rate of adverse events were reported in people with mild or moderate and moderate haemophilia A without inhibitors (83% and 82% respectively).**
Treatment-related adverse events **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, 15/72 (21%) had an adverse event considered related to emicizumab. Most treatment-related adverse events were local injection-site reactions. **(VERY LOW)** **This study provides very low certainty evidence that the majority of emicizumab-related adverse events in people with mild or moderate haemophilia A without inhibitors were local injection-site reactions. Data for people with moderate haemophilia A were not reported separately.**
Serious adverse events **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, 8/72 (11%) had a serious adverse event. None were considered to be emicizumab-related. There were no deaths, no systemic hypersensitivity, anaphylactic, or anaphylactoid reactions and no clinically significant changes from baseline in vital signs or ECG parameters. **(VERY LOW)** • Négrier et al. 2023 showed that in people with moderate haemophilia A without inhibitors, 6/51 (12%) had a serious adverse event. **(VERY LOW)**

	This study provides very low certainty evidence on serious adverse events with emicizumab in people with mild or moderate, or moderate, haemophilia A without inhibitors. None were considered to be emicizumab-related. There were no deaths or anaphylactic reactions.
Grade ≥3 adverse events **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, 4/72 (6%) had a grade 3 or above adverse event. **(VERY LOW)** **This study provides very low certainty evidence on the incidence of grade 3 or above adverse events with emicizumab in people with mild or moderate haemophilia A without inhibitors, but information on the nature of these events is not provided. Data for people with moderate haemophilia A were not reported separately.**
Emicizumab treatment withdrawal, modification, or interruption due to adverse event **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors (n=72), there were no adverse events which led to treatment withdrawal, modification, or treatment interruption. **(VERY LOW)** **This study provides very low certainty evidence that there were no adverse events that led to emicizumab treatment withdrawal, interruption, or modification in people with moderate haemophilia A without inhibitors.**
Thrombotic microangiopathies or thrombotic events **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors (n=72), none had a thrombotic microangiopathy event. **(VERY LOW)** • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, 1/72 (1%) had grade 1 (mild) thrombosed haemorrhoids which were classified as a thrombotic event, not considered to be emicizumab-related. **(VERY LOW)** **This study provides very low certainty evidence that there were no thrombotic microangiopathies in people with moderate haemophilia A without inhibitors on emicizumab. One grade 1 (mild) thrombotic event was reported in people with mild or moderate haemophilia A without inhibitors, which was not considered to be emicizumab-related.**
Treatment-induced anti-drug antibodies **Certainty of evidence:** Very low	One multi-centre, open-label, single-arm study provided non-comparative evidence relating to safety (Négrier et al. 2023, n=72). After a median of 55.6 weeks (IQR 52.3 to 61.6 weeks) follow up on emicizumab treatment: • Négrier et al. 2023 showed that in people with mild or moderate haemophilia A without inhibitors, treatment-induced anti-drug antibodies were detected in 2/72 (3%). There were no bleeds, no injection-site reactions, hypersensitivity, or anaphylactic reactions in either of these 2 people. **(VERY LOW)**

	This study provides very low certainty evidence that 2/72 (3%) people with mild or moderate haemophilia A without inhibitors developed emicizumab-induced anti-drug antibodies, but with no clinical consequence of bleeds, injection-site reactions, hypersensitivity or anaphylactic reactions. Data for people with moderate haemophilia A were not reported separately.
Abbreviations ABR, annualised bleed rate; CI, confidence interval; IQR, interquartile range; SD, standard deviation.	

From the evidence selected, are there any subgroups of patients that may benefit from emicizumab prophylaxis more than the wider population of interest?

Outcome	Evidence statement
Rate of treated bleeding events	One multi-centre, open-label, single-arm study (Négrier et al. 2023) (n=72, 51 with moderate haemophilia A and 21 with mild haemophilia A) provided non-comparative evidence for several subgroups for the model-based ABR for treated bleeds over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks). For participants receiving prophylactic FVIII treatment at baseline (n=37; 25 with moderate haemophilia A and 12 with mild haemophilia A), the model-based ABR for treated bleeds over a median follow up of 55.6 weeks was 0.7 (95% CI 0.36 to 1.34) and for participants on episodic treatment at baseline (n=35), it was 1.2 (95% CI 0.54 to 2.48). Baseline model-based ABRs not reported. No statistical analysis reported. For participants having 1.5 mg/kg once a week maintenance dose (n=25), the model-based ABR for treated bleeds over a median follow up of 55.6 weeks was 1.2 (95% CI 0.50 to 2.73); for those having 3 mg/kg every 2 weeks (n=39), it was 0.7 (95% CI 0.37 to 1.37) and for those having 6 mg/kg every 4 weeks (n=8), it was 1.1 (95% CI 0.17 to 7.61). Baseline model-based ABRs not reported. No statistical analysis reported. For participants with no target joints at baseline (n=48), the model-based ABR for treated bleeds over a median follow up of 55.6 weeks was 0·8 (95% CI 0.44 to 1.45); and for participants with any target joints at baseline (n=24), it was 1.1 (95% CI 0.45 to 2.84). Baseline model-based ABRs not reported. No statistical analysis reported. For male participants (n=69), the model-based ABR for treated bleeds over a median follow up of 55.6 weeks was 0.9 (95% CI 0.54 to 1.51); for female participants (n=3), it was 1.4 (95% CI 0.04 to 44.10); for participants <18 years, it was 1.0 (95% CI 0.03 to 5.63) and for participants ≥18 years, it was 0.9 (95% CI 0.01 to 5.36). Baseline model-based ABRs not reported. No statistical analysis reported. **This study provides evidence for several subgroups on the rate of treated bleeds in people with mild or moderate haemophilia A without inhibitors on emicizumab. However, baseline rates were not reported, the subgroups were small and data for those with moderate haemophilia A were not reported separately. Statistical analyses for comparisons between subgroups were also not reported. Conclusions cannot be drawn on whether there are any subgroups of patients that may benefit from emicizumab prophylaxis more than the wider population of interest.**
Rate of all bleeds	One open-label, single-arm study (Négrier et al. 2023) (n=72, 51 with moderate haemophilia A and 21 with mild haemophilia A) provided non-comparative evidence for several subgroups for the model-based ABR for all bleeds over a median follow up of 55.6 weeks (IQR 52.3 to 61.6 weeks). For participants receiving prophylactic FVIII treatment at baseline (n=37; 25 with moderate haemophilia A and 12 with mild haemophilia), the model-based ABR for all bleeds over a median follow up of 55.6 weeks was 2.2 (95% CI 1.49 to 3.12) compared with 12.2 (95% CI 6.15 to 24.05) over the 24 weeks before study entry. For participants on episodic treatment at baseline (n=35), it was 2.4 (95% CI 1.42

	to 4.09) compared with 8.0 (95% CI 5.68 to 11.13) before study entry. No statistical analysis reported. For participants having 1.5 mg/kg once a week maintenance dose (n=25), the model-based ABR for all bleeds over a median follow up of 55.6 weeks was 1.9 (95% CI 1.27 to 2.96); for those having 3 mg/kg every 2 weeks (n=39), it was 2.1 (95% CI 1.37 to 3.26) and for those having 6 mg/kg every 4 weeks (n=8), it was 4.3 (95% CI 1.42 to 13.32). Baseline model-based ABRs not reported. No statistical analysis reported. For participants with no target joints at baseline (n=48), the model-based ABR for all bleeds over a median follow up of 55.6 weeks was 2.1 (95% CI 1.39 to 3.03); and for participants with any target joints at baseline (n=24), it was 2.7 (95% CI 1.64 to 4.54). Baseline model-based ABRs not reported. No statistical analysis reported. For male participants (n=69), the model-based ABR for all bleeds over a median follow up of 55.6 weeks was 2.1 (95% CI 1.53 to 2.77); for female participants (n=3), it was 9.1 (95% CI 1.42 to 58.67). Baseline model-based ABRs not reported. No statistical analysis reported. **This study provides evidence for several subgroups on the rate of all bleeds in people with mild or moderate haemophilia A without inhibitors on emicizumab. However, baseline rates were not reported for most of the subgroups, the subgroups were small and data for those with moderate severity were not reported separately. Statistical analyses for comparisons between subgroups or differences from baseline were also not reported. Conclusions cannot be drawn on whether there are any subgroups of patients that may benefit from emicizumab prophylaxis more than the wider population of interest.**
Abbreviations ABR, annualised bleed rate; CI, confidence interval; IQR, interquartile range	

In people with moderate haemophilia A without inhibitors, what is the cost-effectiveness of emicizumab prophylaxis compared with current standard care?

Outcome	Evidence statement
Cost-effectiveness	No evidence was identified for this outcome.

From the evidence selected, what doses, frequency and route of administration of emicizumab prophylaxis were used and what was the duration of treatment?

Study	Regimen and duration of emicizumab prophylaxis
Négrier et al. 2023	Emicizumab subcutaneous injection. Loading dose of 3 mg/kg once a week for 4 weeks. Followed by a maintenance dose of either 1.5 mg/kg once a week, 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks. The maintenance dosage regimen was chosen by the study participant. 25/72 (35%) choose 1.5 mg/kg once a week, 39/72 (54%) choose 3 mg/kg every 2 weeks and 8/72 (11%) choose 6 mg/kg every 4 weeks. All participants with suboptimal control of bleeding had the option to increase the emicizumab maintenance dosage to 3 mg/kg once a week (off-label dosage). The primary efficacy and safety analyses were planned to be based only on data collected before a potential up-titration to evaluate the intended maintenance dose. Median follow-up on treatment was 55.6 weeks (IQR 52.3 to 61.6 weeks).
Abbreviations: IQR, interquartile range	

Patient Impact assessment

The Patient Impact form provides additional background information to Clinical Priorities Advisory Group (CPAG) on the impact of the medical condition for which the proposed treatment is indicated. The details below specifically reference the lived experience of patients and caregivers. This supporting information will help CPAG members contextualise the clinical evidence for a treatment or service. It does not change the methodology used to make decisions when considering in year service development policy propositions or policy propositions entered into the prioritisation process.

The condition has the following impacts on the patient's everyday life:

- **mobility:** Patients have variable problems in walking about
- **ability to provide self-care:** Patients have variable problems in washing
- **undertaking usual activities:** Patients can have moderate to severe problems in doing their usual activities
- **experience of pain/discomfort:** Patients can have moderate to severe pain or discomfort
- **experience of anxiety/depression:** Patients can be moderately to extremely anxious or depressed

Further details of impact upon patients:

Patients are severely impacted by both acute and chronic elements of the condition. Acute bleeds can lead to pain, swelling, bruising, and lost days from school and work. Recurrent bleeds impact on joint health, causing arthropathy, reduce range of motion and chronic pain. This can interfere with daily life and restrict mobility. Fears or risks of bleeds can affect participation in general life and activities, such as sports or social events, leading to feelings of depression, isolation and anxiety.

Further details of impact upon carers:

The impact of the disease and managing the treatment required is time-consuming for carers. Caring is time-consuming, with needs increased based on the extent of the patient's joint damage and treatment need. This may impact on the carer's social and work life, leading to lost days from work and carers can become socially excluded and anxious in the same way as patients. Caring for a patient with reduced mobility may become physically exhausting for carers.

Considerations

Equality and Health Inequalities Impact Assessment (EHIA)	
Summary of any potential impacts of the proposal	This policy proposition will make an effective and substantially more convenient, treatment, which is already established as the standard of care for Haemophilia A with severe bleeding phenotype, available to a slightly wider group of patients with Haemophilia A (+~5% of current eligible patient population) with similar bleeding profiles to

	the current eligible patient population. In the absence of emicizumab the only prophylaxis treatment available is intravenous FVIII injected 3 or 4 times per week. Emicizumab is a subcutaneous injection administered once per fortnight in most patients (range once-weekly to 4-weekly). There are no established inequalities across the patient group other than almost all patients with severe or moderate haemophilia A are natal males as the condition is an X-linked chromosomal disorder.

13Q Assessment

PPVAG outcome	No consultation required
Were PPVAG assured of the level of stakeholder testing?	Yes, 3rd Oct 2024, see: PPVAG Assurance Checklist – emicizumab 13Q.

Rare Disease Advisory Group

Not Applicable

Pharmaceutical

Yes

This clinical commissioning policy proposition is for the use of emicizumab for prophylaxis of bleeding episodes in people with moderate haemophilia A without inhibitors in all ages. The recommendation is aligned to the marketing authorisation for emicizumab. Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined in the policy. Emicizumab is on the NHS Payment Scheme Annex A, that is, it is a high-cost drug.

National Programme of Care

Blood and Infection Programme of Care

Assured at POC Assurance Group, 26th Nov 2024