National Institute for Health and Care Excellence

Health Technology Evaluation

Marstacimab for treating severe haemophilia A or severe haemophilia B in people 12 years and over [ID6342]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments	Action
Appropriateness of an evaluation and proposed evaluation route	Pfizer	Yes, it is appropriate to refer marstacimab for a NICE appraisal.	Thank you for your comment. No action needed.
	Roche Products	None	No action needed.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	We have reservations on the appropriateness of evaluating prophylactic and on demand haemophilia treatments through NICE technology appraisals. Considering that all relevant comparators have received reimbursement by NHS Specialised Commissioning and are placed on national frameworks via a tendering process we anticipate equity issues to arise.	Comment noted. This topic has been routed to a Single Technology Appraisal. No action needed.

Section	Stakeholder	Comments	Action
		In addition, historically, there is a paucity of comparative evidence in the haemophilia space and the data that are available are anticipated to not meet NICE's requirements for decision-making.	
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	None	No action needed.
Wording	Pfizer	The population has changed to reflect the Phase 3 BASIS trial [redacted]. Therefore, we suggest the Draft remit/evaluation objective be updated to the following wording: "To appraise the clinical and cost effectiveness of marstacimab within its marketing authorisation for treating severe haemophilia A or ~~moderately severe to~~ severe haemophilia B in people 12 years and over."	Thank you for your comment. The remit has been updated.
	Roche Products	The remit should reflect the population covered by the expected marketing authorisation for marstacimab.	Thank you for your comment. The remit has been updated.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	None	No action needed.

Section	Stakeholder	Comments	Action
Timing issues	Pfizer	It is expected that NICE will schedule committee discussions such that the gap between Marketing Authorisation and final guidance is as short as possible. Timely NICE guidance is crucial to ensure this innovative technology reaches NHS patients quickly.	Comments noted. NICE aims to provide draft guidance to the NHS as close as possible to the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.
	Roche Products	None	No action needed.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	None	No action needed.
Additional comments on the draft remit	Pfizer	n/a	Thank you for your comment. No action needed.
	Roche Products	None	No action needed.
	CSL Behring UK	None	No action needed.

Section	Stakeholder	Comments	Action
	Novo Nordisk	N/A	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	None	No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	Pfizer	As mentioned previously, the population has changed to reflect the BASIS trial [redacted] Therefore, we suggest the following statements within the background section can be updated as follows: ~~"Moderately severe haemophilia does not have a standard definition but is generally considered to be less than 2% of normal clotting factor."~~ "There were 2,069 people in the UK with haemophilia B in 2022/2023, of whom 374 had severe ~~and 351 had moderate~~ disease." "Marstacimab (PF-06741086, Pfizer) does not currently have a marketing authorisation in the UK for treating severe haemophilia A or moderately severe to severe haemophilia B in people 12 years and over. It has been studied in clinical trials in adults and children with previously treated severe haemophilia A or ~~moderately severe to~~ severe haemophilia B.	Thank you for your comment. The wording of the scope has been updated in line with the final remit and population.

Section	Consultee/ Commentator	Comments	Action
	Roche Products	Paragraph 1: It is stated that some people can have haemophilia B without family history of the disease but this is also applicable to haemophilia A - approximately a third of cases. Paragraph 4: Not all treatments require multiple injections per week so suggestion to amend wording to reflect this. Paragraph 3: Reference 2 links to the 2021 UKHCDO report but the data is from the 2023 report so reference at the end of the document requires updating. Paragraph 4: There are two NHS England Clinical Commissioning policies for emicizumab in haemophilia A. One for patients with inhibitors and one for patients without inhibitors. Only one is referenced here so a second reference (reference number 5) should be added.	Thank you for your comment. The wording of the scope has been updated.
	CSL Behring UK	The Draft Scope currently does not distinguish between treatment regimens for haemophilia A and haemophilia B, particularly in the context of extended half-life (EHL) treatments. Haemophilia A EHL treatments typically require multiple injections per week, compared to haemophilia B EHL treatments which start with a dosing schedule of once every 7 days. This discrepancy is rooted in the inherent differences in the half-lives of the clotting factors involved. Given the significant variation, we recommend listing and evaluating the evidence pertaining to haemophilia A and haemophilia B comparator treatments separately.	Thank you for your comment. The background has been updated to highlight the differences in administration frequency between haemophilia A and B.
	Novo Nordisk	Novo Nordisk propose the following amendments: - *Haemophilia is a rare, lifelong genetic condition that affects the ability of blood to clot.* – Add the relevant reference for this sentence, NHS (2020) Haemophilia.	Thank you for your comment. The background has been updated where

Section	Consultee/ Commentator	Comments	Action
		- *Instances of severe haemophilia A or B in women are rare.* – Cite the relevant reference in this sentence, Michele, D et al. (2014). Severe and moderate haemophilia A and B in US. females. Haemophilia. 20(2), e136-43 - *Registry data suggests that in 2022/2023 there were 9,316 people with haemophilia A, including 2,230 with severe disease in the UK.*[2] – Update the reference with the most recent UKHCDO report from 2023. - *There were 2069 people in the UK with haemophilia B in 2022/2023, of whom 374 had severe and 351 had moderate disease.* - Cite the relevant reference in this sentence, UKHCDO report. - *Replacement of the missing clotting factor in the blood through an intravenous infusion of clotting factor concentrate is used as a prophylactic (involving multiple injections per week) and on-demand treatment.* – Some extended half-life factor replacement treatments can be administered prophylactically once weekly. Replace the text in the brackets (involving multiple injections per week) with 'current treatment options offer varying dosing regimens - from multiple per week to once weekly.' *NHS England has a clinical commissioning policy for emicizumab as a further prophylactic treatment option in people with haemophilia A with inhibitors and in people with severe haemophilia A without inhibitors.* – According to topic ID5098, NHS England have confirmed that emicizumab's mild or moderate haemophilia A indication may be considered for routine commissioning. If this indication is covered by the commissioning policy, please update the sentence accordingly.	appropriate to include the relevant sources.
	Genetic Alliance UK	None	No action needed.

Section	Consultee/ Commentator	Comments	Action
	The Haemophilia Society	There is some confusion in this section. It would be better to remove "Haemophilia A and B are the 2 main types of the condition" and replace the first sentnce with "Haemophilia A and B are two rare, lifelong genetic condition that affect the ability of blood to clot." Clotting factors could be described as "proteins" rather than "substances" The sentence "Both conditions are normally inherited but some people can have haemophilia B without family history of the disease" is confusing and slightly wrong. It would be better as "Both conditions are normally inherited but around a third of new cases have no known family history of the disease and may be due to random mutations. The NHD administered by the UKHCDO on behalf of NHS England can provide England specific figures as well as the exact number of people with moderate haemophilia B and levels below 2% (moderately severe). In the final paragraph of the background section there is a comment in brackets that says that prophylactic treatment is administered 2-3 times a week. The actual situation is more complex than that; Infusion frequency will vary based on bleeding phenotype, individual pharmacokinetic (PK) response, product used and type of haemophilia. This will often be every 2-3 days but some people need daily infusions to retain therapeutically effective levels. Management of Haemophilia B with the current standard of care using extended half-life products means infusions are usually now only once a week. efanesoctocog alfa which is currently under consideration by NICE for Haemophilia A will also allow weekly infusions for many patients.	Thank you for your comment. The background has been updated as requested.
Population	Pfizer	As noted above, the population has changed to reflect the BASIS trial [redacted] Therefore, we suggest the Population(s) be updated to the following wording:	Thank you for your comment. The population has been updated.

Section	Consultee/ Commentator	Comments	Action
		"People with severe haemophilia A or severe haemophilia B aged 12 years and over"	
	Roche Products	The population should reflect the expected marketing authorisation for marstacimab.	Thank you for your comment. The population has been updated.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	It is important to understand that an individual's bleeding risk is based on their individual circumstances. For example, diagnosed women may experience debilitating menstrual bleeding but their factor activity may classify them as mild or moderately affected. Therefore, prophylaxis treatments for non-severely affected individuals should be addressed similarly to those with severe haemophilia, taking into account patient preference. Individuals that are at high risk of bleeding, regardless of severity, may benefit from prophylactic treatment to protect joints and spontaneous bleeds particularly during periods of physical activity. It has been shown that adults living with non-severe haemophilia experience joint changes despite low bleeding rates.	Thank you for your comment. The technology will be appraised within its marketing authorisation, and the committee will consider the nature of the population affected by the condition.

Section	Consultee/ Commentator	Comments	Action
	The Haemophilia Society	None	No action needed.
Subgroups	Pfizer	Subgroups suggested in the scope: As mentioned previously, the population has changed to reflect the BASIS trial [redacted] Therefore, the suggested subgroup "severity of haemophilia (moderately severe or severe haemophilia B)" will not be possible. Additionally, the interim clinical study report presents results for participants [redacted]. Therefore, the suggested subgroup "development of inhibitors" may not be feasible.	Thank you for your comment. 'Development of inhibitors' has been retained as a subgroup in the scope, and may be considered if evidence allows.
	Roche Products	Subgroup for severity is only applicable to haemophilia B so suggestion to include this in the main bullet, not only in the brackets afterwards to avoid confusion as population for haemophilia A is severe patients only. If all patients (with and without inhibitors) are within the population then the subgroup wording should be updated to include those with inhibitors present - 'presence or development of inhibitors'	Thank you for your comment. The severity subgroup has been removed in line with the updated population. 'Development of inhibitors' has been retained as a subgroup in the scope , and may be considered if evidence allows.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	Novo Nordisk agree that in principle the subgroups included in the scoping document are relevant to haemophilia. However, it is not clear if the scope includes the entire BASIS phase 3 trial population or solely the without	Thank you for your comment. 'Development of

Section	Consultee/ Commentator	Comments	Action
		inhibitors cohort. If the scope refers to without inhibitors patients only then the with inhibitors subgroup would, by default, be considered out of scope. Alternatively, if the scope covers the whole trial population, we propose that patients with inhibitors are not designated as a subgroup but rather as a distinct population in alignment with the trial's design. Novo Nordisk suggest a clearer definition of the population and consistent alignment of subgroups to reflect this.	inhibitors' has been retained as a subgroup in the scope, and may be considered if evidence allows.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	It is unclear what is meant by previous treatment status. Close to all of the population as defined will have been previously treated with factor replacement products or Emicizumab or both. However, there is no reason we are aware of that would exclude Marstacimab as a first line treatment with previously untreated patients. The population as defined includes people with active inhibitors to FVIII and FIX. There is an effective treatment (Emicizumab) for people with Haemophilia A and inhibitors but the small group of people with Haemophilia B and inhibitors are expensive and difficult to treat (current managed is with rFVIIa (usually Novoseven) and may therefore disproportionately benefit from this treatment if it is a licensed option for them.	Thank you for your comment. 'Previous treatment status' has been removed from the scope. 'Development of inhibitors' has been retained as a subgroup in the scope, and may be considered if evidence allows.
Comparators	Pfizer	Prophylactic factor replacement is the most relevant comparator as established clinical management for the target population, i.e. adults with severe haemophilia A and B. Additionally, patients with haemophilia A may also use emicizumab, a monoclonal antibody (mAb). A very small number of patients who are eligible for prophylaxis may continue to use an on-demand treatment regimen (i.e., factor treatment only at the time of a bleeding event) due to personal preference and clinical challenges with	Thank you for your comment. The comparator for haemophilia A and B has been updated to detail that on demand treatment will only be used with prophylaxis. The comparators listed

Section	Consultee/ Commentator	Comments	Action

		administration of prophylactic treatment. However, guidelines published by the British Society for Haematology (BSH) in 2020 recommend that people with severe haemophilia are treated with primary prophylaxis.[1] In agreement, the World Federation of Hemophilia's (WFH) 2020 Guidelines also recommend that patients with a severe phenotype of haemophilia be on prophylaxis sufficient to prevent all bleeds.[2] Therefore, it is important to note that 'on-demand' treatment is only an appropriate comparator within the context of a prophylactic regimen.
		
		The NICE technology assessments for efanesoctocog alfa, etranacogene dezaparvovec and fidanacogene elaparvovec are currently in progress.[3-5] Therefore, they are not currently considered as established clinical practice in the NHS. Additionally, patients eligible for marstacimab may not be eligible for treatment with gene therapy (e.g., adolescent patients and patients with neutralising antibodies to certain adeno-associated viruses). Therefore, although these therapies may in the future provide alternative options for NHS patients, established NHS clinical management is the most appropriate comparator.
		
		Therefore, we suggest the wording for the 'Comparators' section be updated to the following:
		
		"For people with severe haemophilia A:
		• *Established clinical management, including:*
		  ○ *prophylaxis and on-demand treatment with factor VIII replacement therapy*
		  ○ *emicizumab (in accordance with NHS England's clinical commissioning policy)*
		For people with severe haemophilia B:
			in the scope should be inclusive. Hence, efanesoctocog alfa, etranacogene dezaparvovec and fidanacogene elaparvovec are included subject to ongoing NICE evaluations, in line with the current methods for technology appraisal.

Section	Consultee/ Commentator	Comments	Action
		• *Established clinical management, including:* ○ *prophylaxis treatment with factor IX replacement therapy"* *References provided but not listed here.*	
	Roche Products	For emicizumab there are two NHS England clinical commissioning policies so the word policy should be pluralised.	Thank you for your comment. The scope has been amended as requested.
	CSL Behring UK	We believe appropriate comparators are listed but, as per our comment on the Background Information, the prophylactic dosing frequency for haemophilia B stated is inaccurate. Most patients with haemophilia B are on once weekly dosing with EHLs.	Thank you for your comment. No further action needed.
	Novo Nordisk	Novo Nordisk understand that efanesoctocog alfa is a factor replacement therapy therefore it might be misleading to include it in a separate bullet point. Novo Nordisk recommends incorporating efanesoctocog alfa in the factor replacement therapy category as per following: 'prophylaxis and on-demand treatment with factor VIII replacement therapy (including efanesoctocog alfa - subject to NICE evaluation)'	Thank you for your comment. The scope has been amended as requested.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	For people with haemophilia B and inhibitors is comparator product is rFVIIa, Novoseven.	Thank you for your comment. Giroctocogene

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		Giroctocogene Fitelparvovec and Valoctocogene Roxaparvovec do not have marketing authorisations from the MHRA and therefore are not available in the UK and should not be considered comparators in NICE's assessment of Marstacimab.	fitelparvovec and valoctocogene roxaparvovec are not comparators in the scope. Recombinant activated coagulation factor VII (rFVIIa) (for people with inhibitors) has been added to the scope for people with heamophilia B.
Outcomes	Pfizer	It is Pfizer's understanding that outcomes within the scope are kept broad. Therefore, the outcomes listed here are generally considered appropriate. However, a few outcomes are not considered appropriate: Change in factor IX levels is not a consideration given the mechanism of action of marstacimab does not replace factor levels. Additionally, the sole focus on factor IX excludes factor VIII which is the impacted factor for haemophilia A. Therefore, to reflect the characteristics of the conditions and the outcomes of the BASIS trial more accurately, it is suggested the 'Outcomes' section wording be updated to the following text: *"Outcome measures to be considered include:* • *Annualised bleeding rate* • *Durability of response to treatment* • *Complications of the disease (e.g., joint health)* • *Adverse effects of treatment* • *Health-related quality of life"*	Thank you for your comment. 'Change in factor IX levels' have been removed from the scope. The need for on demand factor VIII injections has been added to the scope.

Section	Consultee/ Commentator	Comments	Action
	Roche Products	Suggest to include the below outcomes as relevant for haemophilia A: change in factor VIII levels need for further treatment with factor VIII injections Suggest to include the below outcome in line with other scopes in this disease	Thank you for your comment. Marstacimab is not expected to alter the factor VIII or IX levels, so these outcomes are not included in the updated scope. The need for on demand factor VIII injections has been added to the scope.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	Novo Nordisk propose the following amendments: - Amend 'change in factor IX levels' to ''change in factor VIII/ or IX levels' - Amend 'need for further treatment with factor IX injections' to 'need for further treatment with factor VIII or IX injections' - Highlight that durability of response to treatment is specific to gene therapy - Amend 'adverse effects of treatment' to 'adverse effects of treatment and development of anti-drug antibodies' - Include annualised joint bleeds in the outcome list.	Thank you for your comment. Marstacimab is not expected to alter the factor VIII or IX levels, so these outcomes are not included in the updated scope. The need for on demand factor VIII injections has been added to the scope. Durability of response has been retained as an outcome for consistency with other

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			haemophilia scopes. Development of anti-drug antibodies will be captured in the listed 'complications of the disease' and annualised joint bleeds captured in 'annualised bleeding rate'.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	This whole section needs to be clear that for Haemophilia A the target is FVIII and for Haemophilia B it is FIX. So for example the first bullet should be change in FVIII or FIX levels as appropriate and he second bullet could be "need for further treatment with factor products. Treatment with a factor product is usually described as an infusion as they are administered intravenously. Treatment with Marstacimab and Emicizumab are by subcutaneous injection. In general it will be harder to compare on the first bullet measure when comparing to products that don't directly change factor levels such as Emicizumab and Marstacimab. It is unclear why durability of response to treatment is a key outcome here. Except for the two Haemophilia B gene therapies (Etranacogene dezaparvovec and Fidanacogene elaparvovec which are currently subject to NICE evaluation) Marstacimab and all the comparator treatments need to be continuously readministered.	Thank you for your comment. Marstacimab is not expected to change the factor VIII or IX levels, so these outcomes are not included in the updated scope. The need for on demand factor VIII injections has been added to the scope. Durability of response has been retained as an outcome for consistency with other haemophilia scopes. Other relevant

Section	Consultee/ Commentator	Comments	Action
		Other patient relevant outcomes that could be included here are pain and mental health. Impact on lifestyle, sport and career as well as days lost from work or school could also be included.	outcomes highlighted in the response will be captured in the listed 'health-related quality of life' outcome.
Equality	Pfizer	The Phase 3 trial, BASIS, did not include females. NICE should aim to ensure that recommendations do not discriminate based on sex. Additionally, NICE should aim to ensure that recommendations do not discriminate against people with HIV or historical hepatitis B or C infection.	Comment noted. The population in the scope covers all people with severe haemophilia A or severe haemophilia B aged 12 years and over. No action needed.
	Roche Products	Female carriers and females with severe haemophilia A (FVIII < 1%), or moderately severe (FIX <2%) or severe haemophilia B (FIX <1%) are rare, but should not be excluded from any guidance developed to avoid any risk of perceived inequality in access between genders	Comment noted. The population in the scope covers all people with severe haemophilia A or severe haemophilia B aged 12 years and over. No action needed.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.

Section	Consultee/ Commentator	Comments	Action
	The Haemophilia Society	As a subcutaneous injection this product may be particularly useful for people with venous access issues due to joint mobility or damage to veins. This people may not currently be on effective prophylaxis, so particular care should be given to considering the benefits in this group of people.	Thank you for your comment. The committee will consider any uncaptured benefits associated with the technology, or benefits for particular groups, as part of the appraisal. No action needed.
Other considerations	Pfizer	The innovative nature of marstacimab should be considered. Factor prophylaxis treatment is associated with a substantial administration burden; the need for frequent self-administered intravenous infusions greatly interferes with an individual's ability to take part in day-to-day activities that others without the condition may take for granted.[1-3] While emicizumab offers a different mechanism of action to factor replacement therapies, patients are still required to draw up their dose prior to injection; this means issues around weight-based dosing and administration may still remain. Additionally, emicizumab is only indicated for those with severe haemophilia A which means an unmet need remains for a subcutaneous prophylactic option for all individuals with severe haemophilia (both haemophilia A and haemophilia B). Marstacimab fills a substantial unmet need for an efficacious therapy with a novel mechanism of action and a convenient and simple method of administration:	Thank you for your comment. The committee will consider the innovative nature of a technology as part of the appraisal. No action needed.

Section	Consultee/ Commentator	Comments	Action
		• Marstacimab is a human monoclonal immunoglobulin G1 (IgG1) antibody, which is self-administered by a prefilled weekly subcutaneous injection. • Furthermore, Marstacimab is administered as a flat dose, further reducing the complexity of administration associated with the weight-based dosage needed for all other available treatments. 1. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia. Haemophilia 2020;26:1-158. 2. Brod M, Bushnell DM, Neergaard JS, et al. Understanding treatment burden in hemophilia: development and validation of the Hemophilia Treatment Experience Measure (Hemo-TEM). Journal of Patient-Reported Outcomes 2023;7:17. van Balen EC, Wesselo ML, Baker BL, et al. Patient perspectives on novel treatments in haemophilia: a qualitative study. The Patient-Patient-Centered Outcomes Research 2020;13:201-210.	
	Roche Products	None	No action needed.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.

Section	Consultee/ Commentator	Comments	Action
	The Haemophilia Society	None	No action needed.
Questions for consultation	Pfizer	Where do you consider marstacimab will fit into the existing care pathway for severe haemophilia A or moderately severe to severe haemophilia B? As noted in the 'Background' and 'Population' sections, the BASIS trial [redacted] Therefore, the moderately severe population is no longer applicable and only the severe population for both haemophilia A and B is relevant. Marstacimab is anticipated to be an additional option for treating severe haemophilia A or severe haemophilia B in people 12 years and over [redacted] Would marstacimab ever be used for on demand treatment of severe haemophilia A or moderately severe to severe haemophilia B? The anticipated indication for marstacimab is for prophylaxis treatment only (i.e., preventing bleeds). Would marstacimab be used in people who would otherwise have factor VIII and IX alone or would it be given later in the pathway? Marstacimab would be used as an alternative prophylactic treatment for Factor VIII replacement, Factor IX replacement, or emicizumab, and is not planned as a treatment option further in the pathway.	Thank you for your comments. Please see answers to previous comments. No further action needed.

Section	Consultee/ Commentator	Comments	Action
		How would people with moderately severe haemophilia B be identified in clinical practice? As noted in the 'Background' and 'Population' sections, [redacted] Therefore, this question is no longer applicable. Would marstacimab be used in untreated people with severe haemophilia A or moderately severe to severe haemophilia B? This scenario would be extremely unlikely because, as mentioned above, both BSH and WFH guidelines recommend treatment for people with severe haemophilia. This aligns with the inclusion criteria of the BASIS trial which required enrolling participants to either be receiving routine prophylaxis or be receiving on-demand treatment that required coagulation factor infusion(s). Would marstacimab be a candidate for managed access? Given any major uncertainties are anticipated to be addressed by the trial evidence, marstacimab is not currently deemed to be a candidate for managed access. Do you consider that the use of marstacimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Health-related quality of life is an important outcome and encapsulates a range of physical, psychological, and social domains. It will be important for this appraisal to consider outcomes beyond just the disutility associated with acute bleeding. For example, current routine prophylaxis is associated with repetitive intravenous infusions that can negatively impact the ability of	

Section	Consultee/ Commentator	Comments	Action
		individuals to fully engage in social and sporting activities, travel, education, and employment. Additionally, anxiety and worrying about bleeding and frequent infusions can have significant psychological impacts.[1] The impact of marstacimab on these quality-of-life domains is important to consider. 1. Buckner TW, et al. Impact of hemophilia B on quality of life in affected men, women, and caregivers—Assessment of patient-reported outcomes in the B-HERO-S study. Eur J Haematol. 2018;100(6):592-602.	
	Roche Products	None	No action needed.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	No comment	Thank you for your comment. No action needed.
	Genetic Alliance UK	None	No action needed.
	The Haemophilia Society	None	No action needed.
Additional comments on the draft scope	Pfizer	n/a	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments	Action
	Roche Products	- Suggestion to amend reference to children in The Technology section to adolescents or people >12 years of age for consistency (children <12 years not in the population) - Related NICE recommendation section requires publication dates to be updated for efanestocog alfa & etranocogene dezaparvovec and suggestion to amend all related recommendations listed to 'expected publication date' - Suggestion to add the following to the Related National Policy section to be consistent with other scopes in this disease area: - NHS England. 2013/14 NHS Standard Contract for haemophilia A (all ages). B05/S/a NHS England. Clinical Commissioning Policy: Emicizumab as prophylaxis in people with severe congenital haemophilia A without factor VIII inhibitors (all ages). 170134P. August 2019. NHS England. Clinical Commissioning Policy: Emicizumab as prophylaxis in people with congenital haemophilia A with factor VIII inhibitors (all ages). 170067/P. July 2018.	Thank you for your comment. The suggested amendments have been made to the scope.
	CSL Behring UK	None	No action needed.
	Novo Nordisk	N/A	Thank you for your comment. No action needed.
	Genetic Alliance UK	We have consulted with the Haemophilia Society and support their response.	Thank you for your comment. No action needed.
	The Haemophilia Society	Any additional comments on the draft scope Where do you consider marstacimab will fit into the existing care pathway for severe haemophilia A or moderately severe to severe haemophilia B?	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments	Action
		This product should be able to be an alternative to the current treatments available for all people in the target population. Would marstacimab ever be used for on demand treatment of severe haemophilia A or moderately severe to severe haemophilia B? Marstacimab can only be used prophylactically. Would marstacimab be used in people who would otherwise have factor VIII and IX alone or would it be given later in the pathway? The product is an alternative to FVIII or FIX prophylaxis or Emicizumab. It can't be used for on demand treatment of bleeds. People on FVIII or FIX prophylaxis or Emicizumab or Marstacimab are given additional FVIII or FIX when needed in response to bleeds, trauma or for surgery. How would people with moderately severe haemophilia B be identified in clinical practice? People with Haemophilia A and B have their levels regularly monitored and will have been tested to know their baseline levels prior to starting treatment. Would marstacimab be used in untreated people with severe haemophilia A or moderately severe to severe haemophilia B?	

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		We are not aware of any reason why this couldn't be a first line treatment for previously untreated people. Do you consider that the use of marstacimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? The burden of treatment is often undervalued. Some people with Haemophilia B will greatly value having a sub-cutaneous treatment option as there is not one at present. This product can also prevent bleeding in people with other bleeding disorders such as VWD or rarer factor deficiencies and platelet disorders. Making it available for its licensed indication may also allow off label use for people with bleeding disorders without good alternative treatment options.	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

None