NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Marstacimab for treating severe haemophilia A or moderately severe to severe haemophilia B in people 12 years and over ID6342

Draft scope

Draft remit/evaluation objective

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.

Background

Haemophilia is a rare, lifelong genetic condition that affects the ability of blood to clot. This is caused by the inability or reduced ability of the body to produce substances called clotting factors which are needed for clotting. Haemophilia A and B are the 2 main types of the condition. In haemophilia A, the factor affected is called factor VIII (eight). In haemophilia B, the factor affected is called factor IX (nine). Both conditions are normally inherited but some people can have haemophilia B without family history of the disease. Instances of severe haemophilia A or B in women are rare.

The main symptom of haemophilia is prolonged bleeding. Other complications can include bleeding into joints and muscles without having had an injury. Severity of haemophilia is classed according to how much clotting factor is missing compared with normal expected levels of clotting factor. Severe haemophilia is classed as having less than 1% of normal clotting factor. Moderately severe haemophilia does not have a standard definition but is generally considered to be less than 2% of normal clotting factor.

It is estimated that there are around 25 cases of haemophilia A per 100,000 male births and 5 cases of haemophilia B per 100,000 male births.[1] 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] There were 2069 people in the UK with haemophilia B in 2022/2023, of whom 374 had severe and 351 had moderate disease.

Current clinical management of haemophilia involves prophylactic treatment to prevent bleeding and long-term damage caused by bleeding. On-demand treatment can be administered in response to bleeding episodes. 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 people with haemophilia develop antibodies to replacement clotting factor, called inhibitors, which makes treatment with clotting factor replacement less effective.[3] 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.[4]

The technology

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.

Intervention(s)	Marstacimab
Population(s)	People with severe haemophilia A or moderately severe to severe haemophilia B aged 12 years and over
Subgroups	If evidence allows subgroups will be considered based on: • severity of haemophilia (moderately severe or severe haemophilia B) • development of inhibitors • previous treatment status

Comparators	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)
	  ○ efanesoctocog alfa (subject to NICE evaluation)
	For people with moderately severe to severe haemophilia B:
	• Established clinical management, including:
	  ○ prophylaxis and on-demand treatment with factor IX replacement therapy
	  ○ Etranacogene dezaparvovec (subject to NICE evaluation)
	  ○ Fidanacogene elaparvovec (subject to NICE evaluation)

Outcomes	The outcome measures to be considered include: • change in factor IX levels • need for further treatment with factor IX injections • annualised bleeding rate • durability of response to treatment • complications of the disease (e.g. joint problems and joint surgeries) • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.

	The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** None. **Related appraisals in development:** Efanesoctocog alfa for treating and preventing bleeding episodes in haemophilia A NICE technology appraisal guidance [ID6170]. Publication date 19 June 2024. Fidanacogene elaparvovec for treating moderately severe to severe haemophilia B NICE technology appraisal guidance [ID4032]. Publication date 14 August 2024. Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B NICE technology appraisal [ID3812]. Publication date September 2023. Valoctocogene roxaparvovec for treating severe haemophilia A Proposed NICE technology appraisal [ID3806] [GID-TA10682]. Publication date to be confirmed. Giroctocogene fitelparvovec for treating moderately severe to severe haemophilia A. Proposed NICE technology appraisal [GID-TA11329]. Publication date to be confirmed. **Related NICE guidelines:** None. **Related NICE guidelines in development:** None. **Related interventional procedures:** None. **Related quality standards:**

	None.
Related National Policy	NHS England (2013) 2013/14 NHS standard contract for haemophilia (all ages) section B part 1 - service specifications The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 132.

Questions for consultation

Where do you consider marstacimab will fit into the existing care pathway for severe haemophilia A or moderately severe to severe haemophilia B?

Would marstacimab ever be used for on demand treatment of severe haemophilia A or moderately severe to severe haemophilia B?

Would marstacimab be used in people who would otherwise have factor VIII and IX alone or would it be given later in the pathway?

How would people with moderately severe haemophilia B be identified in clinical practice?

Would marstacimab be used in untreated people with severe haemophilia A or moderately severe to severe haemophilia B?

Would marstacimab 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?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which marstacimab will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Iorio et al., (2019) Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males. A Meta-analytic Approach Using National Registries.Annals of Internal Medicine. 171(8)

2. United Kingdom Haemophilia Centres Doctors' Association (2021) UKHCDO Annual Report 2021. Accessed March 2022

3. NHS (2020) Haemophilia treatment. Accessed January 2024.

4. NHS England. Emicizumab as prophylaxis in people with severe congenital haemophilia A without factor VIII inhibitors (all ages). Clinical Commissioning Policy 170134P. August 2019. [Accessed January 2024]