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]

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of marstacimab within its marketing authorisation for treating severe haemophilia A or severe haemophilia B in people 12 years and over.

Background

Haemophilia A and B are 2 rare, lifelong genetic conditions that affect the ability of blood to clot. This is caused by the inability or reduced ability of the body to produce proteins called clotting factors which are needed for clotting. 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 about a third of people have no known family history of the haemophilia A or B so the condition may be due to random mutations. Instances of severe haemophilia A or B in women are rare.[1]

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.

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.[2] Registry data suggests that in 2022/2023 there were 9,316 people with haemophilia A, including 2,230 with severe disease in the UK.[3] There were 2,069 people in the UK with haemophilia B in 2022/2023, of whom 374 had severe disease.[3]

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 and on-demand treatment; current prophylactic treatment options have varying dosing regimens from multiple injections per week to once weekly. Some people with haemophilia develop antibodies to replacement clotting factor, called inhibitors, which makes treatment with clotting factor replacement less effective.[4] NHS England has clinical commissioning policies for emicizumab, a subcutaneous treatment, as a further prophylactic option in people with haemophilia A with inhibitors and in people with severe haemophilia A without inhibitors.[5, 6]

The technology

Marstacimab (brand name unknown, Pfizer) does not currently have a marketing authorisation in the UK for treating severe haemophilia A or severe haemophilia B in people 12 years and over. It has been studied in clinical trials in adults and young people with previously treated haemophilia A or haemophilia B.

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

Comparators	For people with severe haemophilia A:
	• Established clinical management, including:
	  ○ prophylaxis (with or without on-demand treatment) with factor VIII replacement therapy (including efanesoctocog alfa - subject to NICE evaluation)
	  ○ emicizumab (in accordance with NHS England's clinical commissioning policies)
	For people with severe haemophilia B:
	• Established clinical management, including:
	  ○ prophylaxis (with or without on-demand treatment) with factor IX replacement therapy
	  ○ etranacogene dezaparvovec (subject to NICE evaluation)
	  ○ fidanacogene elaparvovec (subject to NICE evaluation)
	  ○ recombinant activated coagulation factor VII (rFVIIa) (for people with inhibitors)

Outcomes	The outcome measures to be considered include: • annualised bleeding rate • need for on-demand treatment with factor VIII or IX injections • durability of response to treatment • complications of the disease (e.g. joint problems and joint surgeries) • mortality • 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]. Expected publication date to be confirmed. Fidanacogene elaparvovec for treating moderately severe to severe haemophilia B NICE technology appraisal guidance [ID4032]. Expected publication date 14 August 2024. Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B NICE technology appraisal [ID3812]. Expected publication date to be confirmed . Valoctocogene roxaparvovec for treating severe haemophilia A Proposed NICE technology appraisal [ID3806] [GID-TA10682]. Expected publication date to be confirmed. Giroctocogene fitelparvovec for treating moderately severe to severe haemophilia A. Proposed NICE technology appraisal [GID-TA11329]. Expected 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. 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.

References

1. Michele, D et al. (2014). Severe and moderate haemophilia A and B in US. females. Haemophilia. 20(2)
2. 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)
3. United Kingdom Haemophilia Centres Doctors' Association (2023) UKHCDO Annual Report 2023. Accessed April 2024
4. NHS (2020) Haemophilia treatment. Accessed January 2024.
5. 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
6. NHS England. Emicizumab as prophylaxis in people with congenital haemophilia A with factor VIII inhibitors (all ages). Clinical Commissioning Policy 170067/P. July 2018. Accessed April 2024