**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

# Fidanacogene elaparvovec for treating moderately severe to severe haemophilia B [ID4032]

**Final scope**

## Remit/evaluation objective

To appraise the clinical and cost effectiveness of fidanacogene elaparvovec within its anticipated marketing authorisation for treating moderately severe to severe haemophilia B.

## Background

Haemophilia is a rare, lifelong genetic condition that affects the ability of blood to clot.[1] This is caused by the inability or reduced ability of the body to produce substances called clotting factors which are needed for clotting. In haemophilia B, the factor affected is called factor IX (nine). Haemophilia B is normally an inherited condition but some people can have haemophilia B without family history of the disease. Instances of moderately severe or severe haemophilia B in women are rare.[2]

The main symptom of haemophilia is prolonged bleeding but other complications include bleeding into joints and muscles without having had an injury.[1] Severity of haemophilia is classed according to how much clotting factor is missing compared to normal expected levels of clotting factor.[3] Severe haemophilia is classed as less than 1% of normal clotting factor and moderate haemophilia is classed as between 1% and 5% 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.

The prevalence of haemophilia B is estimated at around 3.8 per 100,000.[3] Registry data suggests that in 2021/2022 there were 242 adults with severe haemophilia B and 271 adults with moderate haemophilia B in the UK.[4]

Current clinical management involves replacing the missing clotting factor IX in the blood through an intravenous infusion of clotting factor concentrate. For more severe haemophilia, this involves regular injections of clotting factor (recommended once or twice weekly) that are used to prevent bleeding (known as prophylaxis). On-demand injections of clotting factor can also be used in less severe haemophilia as an immediate response to bleeding. Some people develop antibodies to the replacement factor IX, called inhibitors, which makes treatment with factor IX replacement less effective.[1] Treatments for people with haemophilia B with factor IX inhibitors include the eradication of the inhibitors (through immune tolerance induction), or bypassing agents which activate the blood clotting system by bypassing the inhibitors.

## The technology

Fidanacogene elaparvovec (brand name unknown, Pfizer) does not currently have a marketing authorisation in the UK for the treatment of haemophilia B. It has been

studied in single arm trials in people with moderately severe to severe haemophilia B (defined as less than or equal to 2% of normal factor IX activity) who do not have current or historic factor IX inhibitors and are negative for neutralising antibodies to variant adeno-associated viruses (AAV) serotype Rh74.

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| **Intervention(s)** | Fidanacogene elaparvovec |
| **Population(s)** | Adults with moderately severe or severe haemophilia B |
| **Comparators** | • Established clinical management (including prophylaxis and on-demand treatment)<br>• Etranacogene dezaparvovec (subject to NICE evaluation) |
| **Outcomes** | The outcome measures to be considered include:<br>• change in factor IX levels<br>• need for further treatment with factor IX injections<br>• annualised bleeding rate<br>• durability of response to treatment<br>• complications of the disease (e.g. joint problems and joint surgeries)<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br>The economic modelling should include the cost associated with diagnostic testing in people with haemophilia B who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation). |

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| **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:**<br>None<br>**Related appraisals in development:**<br>'Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B' NICE technology appraisal [ID3812]. Publication expected September 2023.<br>'Valoctocogene roxaparvovec for treating severe haemophilia A' NICE technology appraisal [ID3806]. Publication date to be confirmed.<br>**Related Guidelines:**<br>None.<br>**Guidelines in development:**<br>None.<br>**Related Interventional Procedures:**<br>None.<br>**Related Public Health Guidance/Guidelines:**<br>None.<br>**Related Quality Standards:**<br>None. |
| **Related National Policy** | NHS England (2013) 2013/14 NHS standard contract for haemophilia (all ages) section B part 1 - service specifications<br>The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 132. |

**References**


1. NHS (2020) Haemophilia. Accessed April 2023
2. Michele, D et al. (2014). Severe and moderate haemophilia A and B in US females. Haemophilia. 20(2), e136-43
3. 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)

4. United Kingdom Haemophilia Centres Doctors' Association (2022) UKHCDO Annual Report 2022. Accessed April 2023