

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Evaluation

Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B [ID3812]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of etranacogene dezaparvovec within its marketing authorisation for treating moderately severe or 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 found in males, but some people can have haemophilia B without family history of the disease. Instances of moderately severe or severe haemophilia B in females 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 2020/2021 there were 247 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

Etranacogene dezaparvovec (brand name unknown, CSL Behring) does not currently have a marketing authorisation in the UK for treating haemophilia B. It has been studied in an open-label clinical trial in adult males with severe or moderately severe

haemophilia B (defined as less than or equal to 2% of normal factor IX activity) who currently have factor IX prophylaxis and who do not have current or historic factor IX inhibitors.

Intervention(s)	Etranacogene dezaparvovec
Population(s)	People with moderately severe or severe haemophilia B
Comparators	Established clinical management (including prophylaxis and on-demand treatment)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The use of etranacogene dezaparvovec is conditional on the presence of a specific biomarker (currently considered confidential by the company). The economic modelling should include the costs associated with diagnostic testing for biomarkers 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).</p>

Other considerations	<p>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.</p>
Related NICE recommendations	<p>Related Technology Appraisals: None.</p> <p>Related appraisals in development: ‘Valoctocogene roxaparvovec for treating severe haemophilia A’ Proposed NICE technology appraisal [ID 3806]. Publication date to be confirmed.</p> <p>Related Guidelines: None.</p> <p>Guidelines in development: None.</p> <p>Related Interventional Procedures: None.</p> <p>Related Public Health Guidance/Guidelines: None.</p> <p>Related Quality Standards: None.</p>
Related National Policy	<p>NHS England (2013) 2013/14 NHS standard contract for haemophilia (all ages) section B part 1 - service specifications</p> <p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 132.</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2-5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

References

1. NHS (2020) [Haemophilia](#). Accessed September 2022
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 (2021) [UKHCDO Annual Report 2021](#). Accessed September 2022