NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B

Draft scope

Draft remit/appraisal 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 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 joint and muscle damage from internal bleeding and bruising.[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.

The prevalence of haemophilia B is estimated at around 1 in 30,000 people.[3] Registry data suggests that in 2019/2020 there were 369 people with severe haemophilia B and 344 people with moderately severe 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 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 (known as episodic treatment). 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 [ITI]), or bypassing agents which activate the blood clotting system by bypassing the inhibitors.

The technology

Etranacogene dezaparvovec (brand name unknown, CSL Behring) is a gene therapy that works by using a harmless viral vector to insert a highly functional copy of the F9 gene into a person's DNA. It is administered as a single intravenous infusion.

Etranacogene dezaparvovec 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.

Intervention	Etranacogene dezaparvovec
Population	People with moderately severe or severe haemophilia B
Comparators	Established clinical management (including prophylaxis and episodic treatment)
Outcomes	The outcome measures to be considered include: • change in factor IX levels • need for further treatment with factor IX injections • bleeding • durability of response to treatment • complications of the disease (e.g. joint problems) • 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 of any managed access arrangement for the intervention will 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 and NICE Pathways	None. **Appraisals in development (including suspended appraisals)**

	'Valoctocogene roxaparvovec for treating severe haemophilia A' Proposed NICE technology appraisal [ID 3806]. Publication date to be confirmed.
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) 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

Questions for consultation

Have the relevant comparators for etranacogene dezaparvovec been included in the scope?

How are the severity criteria used in clinical practice?

Which treatments are considered to be established clinical practice in the NHS for haemophilia B?

What proportions of people would be expected to be treated with prophylaxis and on-demand treatment?

What proportion of people develop factor IX inhibitors? What is current clinical management for factor IX inhibitors in haemophilia B? Would it be expected that patients with factor IX inhibitors could be treated with etranacogene dezaparvovec?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom etranacogene dezaparvovec is expected to be more clinically effective and cost effective or other groups that should be examined separately (e.g. severity or presence of inhibitors)?

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 etranacogene dezaparvovec 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.

Do you consider etranacogene dezaparvovec to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of etranacogene dezaparvovec can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. NHS (2020) Haemophilia. Accessed November 2021

2. Michele, D et al. (2014). Severe and moderate haemophilia A and B in US females. Haemophilia. 20(2), e136-43

3. The Haemophilia Society (2017) Understanding Haemophilia. Accessed November 2021

4. United Kingdom Haemophilia Centres Doctors' Association (2020) UKHCDO Annual Report 2020. Accessed November 2021