Engagement Report

Topic details

Title of policy or policy statement: Allogeneic	Allogeneic haematopoietic stem cell transplant for patients with X-linked cerebral adrenoleukodystrophy (Adults)
Programme of Care:	Blood and Infection
Clinical Reference Group:	Metabolic disorders
URN:	2203

1. Summary

This report summarises the feedback NHS England received from engagement during the development of this policy proposition, and how this feedback has been considered.

2. Background

X-linked adrenoleukodystrophy (X-ALD) is a genetic (inherited) disease that affects the nervous system (brain, spinal cord and nerves throughout the body) and the adrenal glands (small glands located on top of each kidney). X-ALD is caused by mutations (changes) in the ABCD1 gene, which leads to very long chain fatty acids (VLCFA) building up in the body. This can lead to several effects including acute brain inflammation and demyelination (loss of the protective nerve coating), and progressive damage to the brain, spinal cord, nerves and the adrenal glands.

The most severe forms of X-ALD are seen in males. This is because the ABCD1 gene is on the “X” chromosome, which is why the condition is called “X-linked”. Men only have one copy of ABCD1 as they have an “XY” chromosome pattern and will be clinically affected if it is faulty. Women who have the “XX” chromosome pattern can have a working copy of ABCD1, as well as a faulty copy. This means women with X-ALD present at a later age with limited features of the disease which progress at a slower rate compared to males. Women are not known to be affected by C-ALD.

C-ALD develops in approximately 35% of affected males younger than 12 years of age and in a smaller percentage of affected patients 12 years of age or older. Without early treatment, C-ALD leads to permanent disability and death. Median life expectancy in adults after onset is about 4 years. It is not possible to predict which patients will develop C-ALD or when it will occur.

The clinical features of X-ALD are varied, with different aspects of the disease appearing at different times. Males with X-ALD may first present in childhood with adrenal insufficiency (problems with the adrenal gland functioning), which means they need life-long medications. They may also present with a second syndrome of rapid neurological damage due to an inflammatory leukodystrophy (loss of the white matter

within the brain), which can affect learning, behaviour, vision and physical functioning (C-ALD). The third clinical syndrome is a slowly progressive spinal cord disease known as adrenomyeloneuropathy (AMN). AMN normally presents in men in their thirties who may or may not have adrenal insufficiency. AMN leads to stiffness and weakness of the legs, including problems with balance and difficulty controlling bladder and bowel function. Patients end up wheelchair bound and requiring catheterisation (a procedure to empty the bladder). This policy proposition is focused on C-ALD.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is the process of stem cell transplantation performed from a tissue-type matched or mismatched donor. The aim of the treatment is to provide a haematopoietic system which has a normal ABCD1 gene. If successful, this can halt, or slow down, the progression of cerebral disease. Evidence has shown that allo-HSCT is most effective when performed as soon as possible following MRI evidence of cerebral changes that indicate the development of C-ALD. Allo-HSCT is currently commissioned for male paediatric patients with C-ALD.

Allo-HSCT is proposed as a one-off intervention for the treatment of C-ALD, and patients with progressive C-ALD after allo-HSCT would not be eligible for a further round of treatment. However, patients who experience failure to engraft would be eligible for a second transplant, in line with NHS England HSCT (All Ages) Policy (B04/P/a).

3. Engagement

NHS England has a duty under Section 13Q of the NHS Act 2006 (as amended) to 'make arrangements' to involve the public in commissioning. Full guidance is available in the Statement of Arrangements and Guidance on Patient and Public Participation in Commissioning. In addition, NHS England has a legal duty to promote equality under the Equality Act (2010) and reduce health inequalities under the Health and Social Care Act (2012).

The policy proposition was sent for stakeholder testing for 29 days from 12th December 2022 to 9th January 2023. The comments have then been shared with the Policy Working Group to enable full consideration of feedback and to support a decision on whether any changes to the proposition might be recommended.

Respondents were asked the following consultation questions:

- Do you support the proposition for allogeneic haematopoietic stem cell transplant for patients with X-linked cerebral adrenoleukodystrophy to be available through routine commissioning based on the evidence review and within the criteria set out in this document?
- Do you believe that there is any additional information that we should have considered in the evidence review?
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of making this treatment option available?
- Do you have any further comments on the proposal?
- Do you support the Equality and Health Inequalities Impact Assessment?
- Does the Patient Impact Summary present a true reflection of the patient and carers lived experience of this condition?
- Please declare any conflict of interests relating to this document or service area.

A 13Q assessment has been completed following stakeholder testing.

The Programme of Care has decided that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation was not required. This decision has been assured by the Patient Public Voice Advisory Group.

4. Engagement Results

Two responses were received:

- One organisation
- One individual

These responses were in favour of the policy proposition. The individual response felt that additional research was required prior to commissioning. This was noted, but no action was taken as Clinical Panel supports a positive commissioning position based on the evidence in the policy proposition. No changes were made to the policy proposition as a result of this response. The patient group are members of the policy working group.

In line with the 13Q assessment it was deemed that further public consultation was not required.

5. How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group and the Blood and Infection PoC. The following themes were raised during engagement:

Due to the limited number of responses, no key themes were identified as a result of the period of stakeholder testing. The responses were in favour of the proposition and supporting documents.

6. Has anything been changed in the policy proposition as a result of the stakeholder testing and consultation?

No changes have been made to the policy proposition.

7. Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposition?

No.