NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

LentiGlobin for treating transfusion-dependent beta-thalassaemia

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of LentiGlobin within its marketing authorisation for treating transfusion-dependent beta-thalassaemia.

Background

Thalassaemia is the name for a group of inherited blood disorders caused by a genetic mutation of the HBB gene that leads to reduced production of healthy red blood cells and haemoglobin in the body, which is used by red blood cells to carry oxygen around the body. There are two basic groups of thalassaemia: alpha-thalassaemia and beta-thalassaemia. The most severe forms are known as transfusion-dependent thalassaemia (or thalassaemia major) and the least severe forms as non-transfusion-dependent thalassemia (thalassaemia minor). Depending on whether one or both alleles of the HBB gene is affected the disease can be categorised into different genotypes. Total absence of the production of beta globin due to a mutation in both alleles of the HBB gene is called beta-zero (β0/β0) genotype. Thalassaemia causes varying degrees of anaemia, leading to symptoms such as tiredness, weakness, shortness of breath and pale skin caused by the lack of haemoglobin. In transfusion-dependent beta-thalassaemia, haemoglobin production is so reduced that normal growth, development and quality of life can only be achieved by regular red cell transfusions from infancy.

Transfusion-dependent beta-thalassaemia affects around 1 in 100,000 of the population in England.[1] There are currently 813 people diagnosed with transfusion-dependent beta-thalassaemia major in the UK according to the National Haemoglobinopathy Registry [2]. The prevalence of thalassaemia varies considerably across different ethnic communities, mainly affecting people of Mediterranean, South Asian, South East Asian and Middle Eastern origin. In the UK, transfusion-dependent beta-thalassaemia is almost exclusively seen in ethnic minority populations, the largest groups being Cypriot, Indian, Pakistani and Bangladeshi[1].

Transfusion-dependent beta-thalassaemia usually requires lifelong treatment with blood transfusions and medication. The frequency of blood transfusions can vary but is typically every 3 to 4 weeks. Treatment with transfusions can cause too much iron to build up in the body and lead to complications including liver cirrhosis, endocrine complications such as diabetes, sterility, and heart failure. Therefore, chelation therapy (medication to remove excess iron from the body) is also a key component in managing transfusion-dependent beta thalassaemia. The only curative intervention is a haematopoietic stem cell transplant, but these transplants carry significant

risks and are only considered for people under the age of 18 years who have a matching donor (approximately 30% of people with transfusion-dependent beta-thalassaemia).

The technology

LentiGlobin (Bluebird Bio) is an autologous beta-globin gene therapy that comprises a lentiviral vector which inserts functional copies of a beta globin gene, known as β-A^{T87Q} into CD34+ haematopoietic stem cells, ex vivo. The resulting engineered stem cells are then reintroduced to the patient by intravenous infusion. Before the infusion, myeloablative chemotherapy using busulfan is given.

LentiGlobin has a marketing authorisation in the UK. It is indicated for the 'treatment of patients 12 years and older with transfusion-dependent β-thalassaemia who do not have a β0/β0 genotype, for whom haematopoietic stem cell transplantation is appropriate but a human leukocyte antigen-matched related haematopoietic stem cell transplantation donor is not available'.

Intervention	LentiGlobin gene therapy
Population	People with transfusion-dependent beta-thalassaemia with a non-β0/β0 genotype, who are eligible for hematopoietic stem cell transplantation but do not have access to a matched related donor
Comparators	Established clinical management of transfusion-dependent beta-thalassaemia, including blood transfusions and chelating agents
Outcomes	The outcome measures to be considered include: • overall survival • symptoms of anaemia • need for transfusion • iron overload complications (e.g. cardiac, liver and endocrine complications) • growth and development (for children and adolescents) • 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.
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: 'Desferrioxamine, deferiprone and deferasirox for the treatment of chronic iron overload in people with thalassaemia' (suspended appraisal). NICE technology appraisal guidance [ID350].
Related National Policy	NHS England (2016) Clinical Commissioning Policy: Treatment of iron overload for transfused and non transfused patients with chronic inherited anaemias NHS England (2016) Manual for prescribed specialised services 2016/17 Chapter 114 - Specialist haemoglobinopathy services (adults and children) NHS England (2013) 2013/14 NHS standard contract for specialised services for haemoglobinopathy care (all ages) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 East Midlands Specialised Commissioning Group (2011) The National Haemoglobinopathies Project: a guide to effectively commissioning high quality sickle cell and thalassaemia services NHS Sickle Cell and Thalassaemia Screening Programme (2012) Information for healthcare professionals

Questions for consultation

Is the population defined appropriately?

Are the outcomes listed appropriate?

Have all relevant comparators for LentiGlobin been included in the scope?

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 LentiGlobin 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 LentiGlobin 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)?

References

1. Medical Data Services and Solutions (Sept 2016) National Haemoglobinopathy Registry Annual Report 2015/16 [accessed 23/01/2018]

2. NHR Information Service Number of patients by diagnosis and Total diagnosis by gender [accessed 18/05/2018]