NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

LentiGlobin for treating beta-thalassaemia major

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Thalassaemia is the name for a group of inherited blood disorders that cause the body to make fewer healthy red blood cells and less haemoglobin, 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 thalassaemia major and the least severe forms as thalassaemia minor. 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 beta-thalassaemia major, haemoglobin production is so reduced that normal growth, development and quality of life can only be achieved by regular red cell transfusions from infancy.

Beta-thalassaemia major affects around 1 in 100,000 of the population in England.[1] There are currently 873 patients diagnosed with 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, beta-thalassaemia major is almost exclusively seen in ethnic minority populations, the largest groups being Cypriot, Indian, Pakistani and Bangladeshi[1].

Beta-thalassaemia major 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 beta thalassaemia major. The only curative intervention in beta-thalassaemia major is a stem cell transplant, but these carry significant risks and are only considered for a small number of patients who have a matching donor.

The technology

LentiGlobin (Bluebird Bio) is a beta-globin gene therapy that comprises a lentiviral vector which inserts a functioning version of the beta globin gene

into a patient's hematopoietic stem cells ex vivo. The resulting engineered stem cells are then reintroduced to the patient by intravenous infusion.

LentiGlobin does not currently have a marketing authorisation in the UK for treating beta-thalassaemia major. It has been studied in single arm studies in people aged 12 to 50 years with beta-thalassaemia major who need at least 100ml/kg or more than 8 blood transfusions per year and who are eligible for hematopoietic stem cell transplantation but do not have access to a matched family donor.

Intervention	LentiGlobin gene therapy
Population	People with beta-thalassaemia major who are eligible for hematopoietic stem cell transplantation but do not have access to a matched related donor
Comparators	Established clinical management of beta-thalassaemia major including blood transfusions and chelating agents
Outcomes	The outcome measures to be considered include: • overall survival • symptoms of anaemia • need for transfusion • adverse effects of treatment • complications of hematopoietic stem cell transplantation • 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]. Publication date to be confirmed.
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?
How many people are living with beta-thalassaemia major who are eligible for hematopoietic stem cell transplantation but do not have access to a matched related donor?
How many people are diagnosed each year with beta-thalassaemia major who are eligible for hematopoietic stem cell transplantation but do not have access to a matched related donor?

Will LentiGlobin be used for specific genotypes of beta-thalassaemia major?

Will diagnostic testing need to be carried out to identify patients eligible for treatment with LentiGlobin? Is the testing already established in clinical practice?

In clinical practice how is LentiGlobin likely to be used? Will it be used with a chemotherapy conditioning regimen?

How will LentiGlobin be delivered in clinical practice? Will its use be restricted to specialist centres or highly specialised centres?

What age groups would be considered for treatment with LentiGlobin? Will it be used in adults and children?

Have all relevant comparators for LentiGlobin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for beta-thalassaemia major? Is hematopoietic stem cell transplantation a relevant comparator for any groups of patients?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom LentiGlobin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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)?

Do you consider that the use of LentiGlobin 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. 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 23/01/2018]