NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Luspatercept for treating beta-thalassaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Thalassaemia is a group of hereditary blood disorders caused by a genetic mutation of the hemoglobin subunit beta (HBB) gene. The condition is characterised by 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.[1] There are two basic groups of thalassaemia: alpha-thalassaemia and beta-thalassaemia.[2] Beta-thalassaemia comprises of several phenotypes with different severity. Beta-thalassaemia major is the most severe type which is transfusion-dependent requiring regular red blood cell (RBC) transfusions. Other types include beta-thalassaemia intermedia, beta-thalassaemia minor as well as beta-thalassaemia with associated hemoglobin (Hb) anomalies such as HbE/Beta-thalassaemia.[3]

Symptoms of beta-thalassaemia vary depending on the severity of the condition. Intermediate forms can cause moderate anaemia and iron overload while people with severe forms experience severe anaemia, iron overload, poor appetite, paleness and weakness caused by the lack of haemoglobin and enlarged liver or heart.[1] In transfusion-dependent beta-thalassaemia, haemoglobin production is reduced to such a low level that normal growth, development and quality of life can only be achieved by regular red cell transfusions from infancy. The most severe cases can lead to heart failure or liver complications.[3]

There are currently 1,351 people diagnosed with beta-thalassaemia in the UK according to the National Haemoglobinopathy Registry. Among them, 970 have beta-thalassaemia major, 243 beta-thalassaemia intermedia and 138 beta-thalassaemia/Hb E disease.[4] 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, the highest prevalence of beta-thalassaemia is seen in ethnic minority populations, the largest groups being Indian, Pakistani and Bangladeshi.[5]

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 an excess of iron to build up in the body leading to complications including liver cirrhosis, endocrine complications such as diabetes, sterility, and heart failure.

Therefore, chelation therapy that removes excess iron from the body is also a key component in managing beta-thalassaemia of greater severity where transfusion is frequently required. The only curative intervention is a haematopoietic stem cell transplant, but these transplants carry significant risks and are only considered for people who have a matching donor.[1]

The technology

Luspatercept (Unknown brand name, Celgene) is a recombinant engineered protein designed to attach to certain proteins that inhibit the maturation of blood cells. It is administered subcutaneously.

Luspatercept does not currently have a marketing authorisation in the UK for any indication. Luspatercept is being studied in a randomised placebo-controlled clinical trial in adults with beta-thalassaemia who require regular red blood cell transfusion.

Intervention(s)	Luspatercept
Population(s)	Adults with beta-thalassaemia who require regular red blood cell transfusion
Comparators	• Established clinical management of transfusion-dependent beta-thalassaemia (including blood transfusions and chelating agents) • Best supportive care
Outcomes	The outcome measures to be considered include: • change in red blood cell transfusion frequency • change in transfusion dependence • change in iron concentration (for example, in liver, cardiac, and endocrine systems) • change in dosing of iron chelation therapy • change in serum ferritin • change in bone mineral density • adverse events and complications • 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 and NICE Pathways	Appraisals in development (including suspended appraisals) Desferrioxamine, deferiprone and deferasirox for the treatment of chronic iron overload in people with thalassaemia [ID350] (suspended appraisal). NICE technology appraisal guidance LentiGlobin for treating beta-thalassaemia major [ID968] Proposed Technology appraisal, Publication date to be confirmed
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2016) Clinical Commissioning Policy: Treatment of iron overload for transfused and non transfused patients with chronic inherited anaemias NHS England (2018/2019) Manual for prescribed specialised services 2018/2019 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: Domains 1, 2, 4, 5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England – Service specification NHS Sickle cell and Thalassaemia Screening Programme (2018-2019) Standard for the Clinical Care of Children and Adults with Thalassaemia in the UK. Thalassaemia Society

	2016

Questions for consultation

Is the population defined appropriately?
The company's pivotal trial included people with beta-thalassaemia who are transfusion dependent requiring regular blood cell transfusion. How is transfusion dependent defined in practice?

Have all relevant comparators for luspatercept been included in the scope? Which treatments are considered to be established clinical practice in the NHS for beta-thalassaemia?

Where does luspatercept fit in the treatment pathway? Would luspatercept be used after transfusion, in addition to transfusion or instead of transfusion?

Are the outcomes listed appropriate? Are there any other outcomes that should be included?

Are there any subgroups of people in whom luspatercept 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 luspatercept 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 luspatercept 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 luspatercept 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 conditions (2016). Thalassaemia [accessed 05/04/2019]

2. Porter J, Taher A, Mufarrij A. et al. Emergency management of thalassaemia (2012) Thalassaemia International Federation [accessed 05/04/2019]

3. Galanello R. and Origa R (2010). Beta-thalassaemia. *Orphanet Journal of Rare Diseases*. 5:11. Available from doi: 10.1186/1750-1172-5-11 [accessed 05/04/2019]

4. NHR Information service (2019) Number of patients by diagnosis and NHR Data and reports [accessed 13/05/2019]

5. Medical Data Services and Solutions (2017) National Haemoglobinopathy Registry Annual Report 2017/2018 [accessed 07/03/2019]