NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Luspatercept for treating beta-thalassaemia

Final scope

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, usually administered every 2 to 5 weeks.[3] Other types include beta-thalassaemia intermedia, beta-thalassaemia minor as well as beta-thalassaemia with associated hemoglobin (Hb) anomalies such as HbE/Beta-thalassaemia.[4] Some people with severe forms of beta-thalassaemia intermedia and HbE/Beta-thalassaemia also require blood transfusions.[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.[4]

The National Haemoglobinopathy Registry reports 1,380 people diagnosed with beta-thalassaemia in the UK as of June 2019. Among them, 996 have beta-thalassaemia major, 246 beta-thalassaemia intermedia and 138 beta-thalassaemia/Hb E disease.[5] 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.[6]

Beta-thalassaemia usually requires lifelong treatment with blood transfusions and medication. 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, the TGF-beta 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 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 red blood cell transfusion units • change in transfusion dependence • change in iron levels (for example, serum ferritin concentration and concentration in liver, cardiac, and endocrine systems) • change in dosing of iron chelation therapy • overall survival • 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 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 Zynteglo for treating transfusion dependent beta-thalassaemia [ID968] Proposed Technology appraisal, Publication date to be confirmed Luspatercept for treating anaemia caused by myelodysplastic syndromes [ID1550] 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

References

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4. 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 October 2019.
5. NHR Information service (2019) Number of patients by diagnosis and NHR Data and reports. Accessed October 2019.
6. Medical Data Services and Solutions (2017) National Haemoglobinopathy Registry Annual Report 2017/2018. Accessed October 2019.