NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Luspatercept for treating anaemia caused by myelodysplastic syndromes

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of luspatercept within its marketing authorisation for treating anaemia caused by myelodysplastic syndromes.

Background

Anaemia is defined as a reduction of haemoglobin concentration, red cell count or packed cell volume to below normal levels. The World Health Organisation has defined anaemia as a haemoglobin level of less than 120 g/L in women and less than 130 g/L in men[1]. Symptoms of anaemia include fatigue, and breathlessness (dyspnoea), particularly on exertion[2].

Myelodysplastic syndromes (MDS) are a diverse group of haematological disorders in which the bone marrow functions abnormally and insufficient numbers of mature blood cells are produced. Red blood cells, white blood cells and platelets may all be affected by MDS, resulting in life threatening disease, with anaemia and increased risk of bleeding and infections. MDS affects quality of life due to debilitating symptoms such as fatigue and dyspnoea, treatment regimens involving hospitalisation with blood transfusions, and complications such as severe infections[3]. The Revised International Prognostic Scoring System (IPSS-R) classifies prognosis as very low-risk, low-risk, intermediate-risk, high-risk or very high-risk based on blood cell levels, cytogenetic factors and number of immature cells (blasts) in the bone marrow and blood[4].

The annual incidence of MDS is estimated at 4 per 100,000, but incidence increases with age and is 30 per 100,000 per year in people over 70 years of age[2]. In 2017, there were 2,385 people newly diagnosed with MDS in England, with over 91% of patients aged over 60 at the time of diagnosis[5]. Most people with MDS will have anaemia at some stage; 40% at diagnosis and 80% during the course of their disease[1].

Killick et al. (2013) states that erythropoiesis-stimulating agents should be used to treat anaemia caused by low to intermediate risk MDS, if the person meets the criteria predicting response to these agents[6]. The alternative treatment option is best supportive care which includes regular red blood cell transfusions. However, this can lead to an accumulation of iron which can cause organ damage in people who have frequent or multiple transfusions. An iron chelator may be used to remove excess iron from the body in these cases. Other supportive treatment, such as platelets, antibiotics and other drugs may also be used due to the complications associated with the disease.

The technology

Luspatercept (Reblozyl, Celgene) is an erythroid (red blood cell) maturation agent (EMA) that stimulates erythropoiesis (formation of red blood cells). It is administered by subcutaneous injection.

Luspatercept does not currently have a marketing authorisation in the UK for treating anaemia caused by MDS. It has been studied in clinical trials in adults with low or intermediate-1 risk MDS who have anaemia. It is also being studied in adults with anaemia caused by very low, low or intermediate risk MDS with ring sideroblasts who require red blood cell transfusions and who have previously received, are not eligible for, or have a low chance of response (based on erythropoietin levels > 200 IU/L) to erythropoiesis-stimulating agent therapy.

Intervention	Luspatercept
Population	Adults with anaemia caused by MDS with ring sideroblasts, isolate deletion 5q cytogenetic abnormality negative and: • are refractory or intolerant to erythropoiesis-stimulating agent therapy • are erythropoiesis-stimulating agent therapy-naïve with a low chance of response to erythropoiesis-stimulating agent therapy.
Comparators	• Best supportive care (including red blood cell transfusions) For patients who are erythropoiesis-stimulating agent therapy-naïve: • erythropoiesis-stimulating agent therapy • best supportive care (including red blood cell transfusions)
Outcomes	The outcome measures to be considered include: • red blood cell transfusion independence and burden • haematological response to treatment • disease progression • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
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	Related Technology Appraisals: Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality (2014) NICE technology appraisal guidance TA322 Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy (2014) NICE technology appraisal guidance TA323 Related Guidelines: Haematological cancers: improving outcomes (2016) NICE guidelines NG47 Related NICE Pathways: Blood conditions (last updated 22 March 2016) NICE pathway
Related National Policy	NHS England. (2015) Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. Reference NHS England B04/P/a. Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 The NHS Long Term Plan, 2019. NHS Long Term Plan

References

1. World Health Organisation. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity (2011). Accessed November 2019.

2. Guidelines for the Diagnosis and Management of Adult Myelodysplastic Syndromes; British Committee for Standards in Haematology (2013). Accessed: November 2019.

3. Synopsis of causation: myelodysplastic syndromes and acute myeloid leukaemia. Ministry of defence (2008). Accessed: March 2019

4. Greenberg PL, Tuechler H, Schanz J et al. (2012) Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes. Blood 120: 2454-2465.

5. Office for National Statistics. Cancer registration statistics, England, 2017. Accessed: November 2019.

6. Killick S.B., Carter C, Culligan D et al. (2013) Guidelines for the diagnosis and management of adult myelodysplastic syndromes. British Journal of Haematology 164, 503-525