NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Luspatercept for treating anaemia caused by myelodysplastic syndromes

Draft scope (pre-referral)

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]

Anaemia is a common symptom of myelodysplastic syndromes (MDS). 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 intravenous drug infusions and 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, 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 2016, there were 2,163 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].

Erythropoiesis-stimulating agents are 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. This includes regular red blood cell transfusions. An iron chelator may also be included to avoid the long-term complications associated with transfusions.

The technology

Luspatercept (brand name unknown, 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 received, are not eligible for, or are intolerant to, erythropoiesis-stimulating agent therapy.

Intervention(s)	Luspatercept
Population(s)	Adults with anaemia caused by MDS and have received or are not eligible for erythropoiesis-stimulating agent therapy.
Comparators	• Best supportive care (including red blood cell transfusions) For low or intermediate-1 risk MDS associated with an isolated deletion 5q cytogenetic abnormality: • Lenalidomide
Outcomes	The outcome measures to be considered include: • red blood cell transfusion independence • 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.

	The use of luspatercept is conditional on the presence of ring sideroblasts. The economic modelling should include the costs associated with diagnostic testing for ring sideroblasts in people with MDS who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
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

Questions for consultation

- What treatment options are available for people who:
    - have not responded to treatment with an ESA?
    - are intolerant to ESAs?
    - are not eligible to receive an ESA?

- How many people would you anticipate being eligible for luspatercept (i.e. with MDS and who have not responded to, or are intolerant to, ESAs?)

- Have all relevant comparators for luspatercept been included in the scope?

- How should best supportive care be defined?

- Are the outcomes listed appropriate?

- 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?

- Where do you consider luspatercept will fit into the existing NICE pathway, Blood conditions?

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 darbepoetin alfa 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. World Health Organisation. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity (2011). Accessed March 2019.

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

3. Gov.uk. Synopsis of causation: myelodysplastic syndromes and acute myeloid leukaemia. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/384518/acute_myeloid_leukaemia_myelodysplastic_syndromes.pdf 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, 2016. Accessed: March 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

