NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Roxadustat for treating anaemia in adults with chronic kidney disease

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of roxadustat within its marketing authorisation for treating anaemia in adults with chronic kidney disease.

Background

Anaemia in chronic kidney disease (CKD) contributes significantly to the burden of CKD. It is defined as a state in which the quality or quantity of circulating red blood cells is below normal. A major cause of anaemia in CKD is a reduction in erythropoietin production because of kidney damage. Erythropoietin stimulates the bone marrow to produce red blood cells (erythropoiesis), and it is made by the kidney in response to low tissue oxygen levels. Other factors that can contribute to development of anaemia in CKD include blood loss (for example, from haemodialysis), a reduced ability to absorb and use iron to make new red blood cells, and inflammation and infection which can suppress the bone marrow[1]. Possible adverse effects of anaemia include reduced oxygen use, increased cardiac output, left ventricular hypertrophy, reduced cognition and concentration, reduced libido and reduced immune responsiveness.

Blood haemoglobin concentration is a key indicator for anaemia because it can be measured directly and has an international standard. NICE guideline 8 (NG8) recommends that clinicians consider investigating and managing anaemia in CKD if a patient's haemoglobin level falls to 110 g/litre or less (or 105 g/litre or less if the patient is younger than 2) or they develop symptoms of anaemia such as tiredness, shortness of breath, lethargy and palpitations.

CKD is divided into 5 stages which increase in severity. The prevalence of anaemia increases progressively with each CKD stage. The Health Survey for England (2016) found that 13% of adults (16 years and over) had CKD (stages 1 to 5). The prevalence of stage 3 to 5 CKD was 5% for all adults, rising to 34% in people aged 75 and over[2]. A cross-sectional study based on data from the Quality Improvement in Chronic Kidney Disease trial, which was conducted in 127 practices from localities across England (2013), reported that the prevalence of anaemia in people with CKD stage 3–5 is 8.6%[3].

Anaemia associated with CKD is potentially reversible with appropriate treatment such as erythropoiesis-stimulating agents (ESAs), iron therapy, or both, depending on the cause of the anaemia. NG8 recommends ESA therapy, for people who are likely to benefit in terms of quality of life and physical function. NG8 does not recommend any specific ESAs, but states that the choice of treatment should take into consideration the patient's dialysis status, the route of administration and local availability. ESA therapy should not be initiated in the presence of absolute iron deficiency without also managing the iron deficiency. In addition, iron therapy should be offered to people who are iron deficient and who are not on ESA therapy. Blood transfusions may be clinically indicated in some situations, for example where there

is ESA resistance. The recommendations in NG8 are consistent with the most recent clinical guidance published by The Renal Association (2017)[4].

The technology

Roxadustat (Evrenzo, Astellas Pharma Ltd) works by binding to prolyl hydroxylase enzymes preventing the breakdown of hypoxia-inducible factor (HIF) and increasing HIF activity. Increased HIF activity leads to erythropoietin production, which in turn causes erythropoiesis and can also lead to increased iron uptake by reducing the expression of the peptide hormone hepcidin, which regulates the absorption of iron into the bloodstream. Roxadustat is administered orally.

Roxadustat does not currently have a marketing authorisation in the UK for treating anaemia in people with CKD. Roxadustat has been studied in a number of randomised controlled trials: four were conducted in patients with stage 3 to 5 disease who were not receiving dialysis (non-dialysis dependent). In one, the comparator was erythropoiesis stimulating agent (ESA) therapy, and in three the comparator was placebo. Four further trials included participants with end-stage renal disease and were receiving dialysis, compared with ESA therapy.

Intervention	Roxadustat
Populations	• Adults with anaemia associated with CKD
Comparators	Erythropoietic stimulating agents
Outcomes	The outcome measures to be considered include: • haemoglobin response • maintenance of haemoglobin levels • use of additional therapy (including blood transfusion and intravenous iron) • hospitalisation • mortality • adverse effects of treatment including major adverse cardiovascular events • 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: None Related Guidelines: Chronic kidney disease: managing anaemia (2015). NICE guideline 8. Last reviewed April 2017. This guideline is being partially updated by the Chronic kidney disease: assessment and management (update) Chronic kidney disease in adults: assessment and management (2015) NICE clinical guideline 182. This guideline is being partially updated by the Chronic kidney disease: assessment and management (update) Guidelines in development Chronic kidney disease: assessment and management (update). Publication expected July 2021. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15. Adult specialist renal services Related Quality Standards: Chronic kidney disease in adults (2017) NICE quality standard 5 Related NICE Pathways: Anaemia management in people with chronic kidney disease overview (2017) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5.

	https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 National Service Frameworks Renal Services

References

1 Kidney Research UK Anaemia and kidney disease. Accessed June 2020.

2 Health survey for England, 2016. Accessed June 2020

3 Dmitrieva O, de Lusignan S, Macdougall IC, et al. Association of anaemia in primary care patients with chronic kidney disease: cross sectional study of quality improvement in chronic kidney disease (QICKD) trial data. *BMC Nephrol*. 2013;14:24. Published 2013 Jan 25. doi:10.1186/1471-2369-14-24

4 Mikhail A, Brown C, Williams JA, et al. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. *BMC Nephrol*. 2017;18(1):345. Published 2017 Nov 30. doi:10.1186/s12882-017-0688-1

