

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Daprodustat for treating anaemia in adults with chronic kidney disease

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of daprodustat 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 marrow¹. Adverse effects of anaemia include reduced oxygen use, fatigue, increased cardiac output, left ventricular hypertrophy, reduced cognition and concentration, reduced libido and reduced immune responsiveness¹.

Blood haemoglobin concentration is a key indicator for anaemia because it can be measured directly and has an international standard. NICE guideline 203 (NG203) 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 defined by evidence of kidney damage, level of renal function as measured by glomerular filtration rate (GFR), and degree of albuminuria. 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 over². 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%^{2,3}.

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. NG203 recommends ESA therapy, for people who are likely to benefit in terms of quality of life and physical function. NG203 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 of ESAs. 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 but are avoided where possible in people with anaemia of CKD in whom a kidney transplant is a treatment option.

The technology

Daprodustat (Jesduvroq, GlaxoSmithKline UK Ltd) is a hypoxia-inducible factor prolyl hydroxylase inhibitor. Inhibition of oxygen-sensing prolyl hydroxylase enzymes stabilises hypoxia-inducible factors, which can lead to transcription of erythropoietin and other genes involved in the production of red blood cells and iron metabolism, similar to the physiological effects that occur in the body at high altitude. Daprodustat is administered orally.

Daprodustat does not currently have marketing authorisation in the UK for treating anaemia in people with CKD. It has been studied in a number of randomised controlled trials compared with ESAs or placebo in adults with anaemia associated with chronic kidney disease. Some of the trials included people who were having dialysis and some included people who were not having dialysis.

Intervention(s)	Daprodustat
Population(s)	Adults with anaemia associated with chronic kidney disease
Subgroups	<p>If evidence allows the following subgroups will be considered</p> <ul style="list-style-type: none"> • Adults with anaemia associated with chronic kidney disease having dialysis • Adults with anaemia associated with chronic kidney disease not having dialysis
Comparators	<ul style="list-style-type: none"> • Erythropoiesis stimulating agents • Roxadustat [subject to ongoing appraisal] <p>For people who cannot have erythropoiesis stimulating agents</p> <ul style="list-style-type: none"> • Established clinical practice without erythropoiesis stimulating agents

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
Other considerations	<p>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.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>None</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Roxadustat for treating anaemia in people with chronic kidney disease. NICE technology appraisal guidance ID 1483. Publication expected July 2022</p> <p>Related Guidelines:</p> <p>Chronic kidney disease: assessment and management (update). (2021) NICE guideline 203.</p> <p>Related Quality Standards:</p> <p>Chronic kidney disease in adults (2017) NICE quality standard 5</p>

<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15. Adult specialist renal services.</p> <p>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</p> <p>National Service Frameworks Renal Services</p>

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