

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Roxadustat for treating anaemia in people with chronic kidney disease

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of roxadustat within its marketing authorisation for treating anaemia in people 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. 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 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%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 (brand name unknown, 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 anemia in people with CKD. It has been compared with placebo in 3 international randomised controlled trials (RCTs) in patients with stage 3 to 5 disease who are not receiving dialysis. It has also been compared with ESA therapy in 4 further international RCTs; in 1 of these studies patients had grade 3 to 5 disease and were not on dialysis, in the remaining 3 the participants had end-stage renal disease and were receiving dialysis.

Intervention(s)	Roxadustat
Population(s)	People with anaemia associated with CKD
Comparators	Established clinical management without roxadustat including erythropoietic stimulating agents and iron therapy
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • haemoglobin response • maintenance of haemoglobin levels • use of rescue therapy • hospitalisation • 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>If the evidence allows subgroups relating to dialysis use (people who do and do not receive dialysis treatment for CKD) will be considered.</p> <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 and NICE Pathways	<p>Related Technology Appraisals:</p> <p>None</p> <p>Related Guidelines:</p> <p>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)</p> <p>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)</p> <p>Guidelines in development</p> <p>Chronic kidney disease: assessment and management (update). Publication expected March 2021.</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15. Adult specialist renal services</p> <p>Related Quality Standards:</p> <p>Chronic kidney disease in adults (2017) NICE quality standard 5</p> <p>Related NICE Pathways:</p> <p>Anaemia management in people with chronic kidney disease overview (2017) NICE pathway</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</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>

Questions for consultation

Is the population defined appropriately?

Is roxadustat a suitable treatment for patients who are iron deficient? Would patients be offered roxadustat in conjunction with iron therapy?

Have all relevant comparators for roxadustat been included in the scope? What treatments are considered to be established clinical practice in the NHS for treating anaemia in people with CKD? Which treatments would be likely to be displaced if roxadustat is recommended?

Are the outcomes listed appropriate? Are there any other key clinical or patient outcomes that should be included?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom roxadustat is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider roxadustat will fit into the existing NICE pathway [Anaemia management in people with chronic kidney disease overview](#) (2017)?

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 roxadustat 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 roxadustat 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 roxadustat 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/pmq19/chapter/1-Introduction>).

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