NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Vadadustat for treating anaemia in adults with chronic kidney disease [ID3821]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of vadadustat 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[1].

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 years) or they develop symptoms of anaemia such as tiredness, shortness of breath, lethargy and palpitations.

Glomerular filtration rate (GFR) is another indicator for anaemia. If the estimated glomerular filtration rate (eGFR) is between the 30 and 60 ml/min/1.73 m^2 threshold, then the extensiveness of investigating causes of anaemia other than CKD, is decided by clinical judgement.

CKD is divided into 5 stages defined by evidence of kidney damage, level of renal function as measured by GFR, and albumin to creatinine ratio. 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%[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, before discussing ESA therapy. In some cases, resistance to ESAs can occur, where the management of the condition will be reviewed. 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

Vadadustat (brand name unknown, Otsuka Pharmaceuticals UK Ltd) is a hypoxia inducible factor prolyl hydroxylase inhibitor. It inhibits the breakdown of hypoxia inducible factor α proteins, which are involved in cell survival under low and very low oxygen concentration levels, through erythropoietin synthesis and iron metabolism. Vadadustat is administered orally.

Vadadustat does not currently have a 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 darbepoetin alfa, an ESA, in adults with anaemia associated with CKD. These trials included people with dialysis dependent CKD and non-dialysis dependent CKD.

Intervention(s)	Vadadustat
Population(s)	Adults with anaemia associated with chronic kidney disease
Subgroups	If the evidence allows subgroups relating to dialysis use will be considered.
Comparators	• Erythropoiesis stimulating agents • Roxadustat (subject to ongoing appraisal)
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. The availability and cost of biosimilar and generic products should 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	**Related Technology Appraisals:** None. **Related appraisals in development:** Roxadustat for treating anaemia in people with chronic kidney disease. NICE technology appraisal guidance [ID1483]. Publication expected June 2022. Daprodustat for treating anaemia in people with chronic kidney disease. NICE technology appraisal guidance [ID3987]. Publication date to be confirmed. **Related Guidelines:** Chronic kidney disease: assessment and management (update) (2021) NICE guideline 203. Renal replacement therapy and conservative management (2018) NICE guideline 107. **Related Quality Standards:** Chronic kidney disease in adults (2017) NICE quality standard 5.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15. Adult specialist renal services. 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

Questions for consultation

Is the population defined appropriately?

Where do you consider vadadustat will fit into the existing care pathway for anaemia in chronic kidney disease?

Is vadadustat a suitable treatment for people who have iron deficiency? Would people be offered vadadustat in conjunction with iron therapy?

Have all relevant comparators for vadadustat been included in the scope? Which 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 vadadustat is recommended?

Which ESAs are considered to be established clinical practice in the NHS for treating anaemia in people with CKD?

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

Is there a group of people who could be treated with vadadustat for whom ESA therapy is not suitable? If so, what treatments do these people currently have?

Are the outcomes listed appropriate? Are there any other key clinical patient outcomes that are currently missing from the scope?

Would vadadustat be a candidate for managed access?

Do you consider vadadustat 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 vadadustat can result in any potential 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 committee to take account of these benefits.

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 vadadustat 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

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