National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Roxadustat for treating anaemia in adults with chronic kidney disease ID1483

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments	Action
Appropriateness	Astellas	Astellas believes that this is an appropriate topic for referral to NICE Roxadustat is a first in class medicine and represents a new treatment approach for patients with anaemia of chronic kidney disease (CKD), with a licence expected in 2021 Evidence has been collected across 8 Phase III clinical trials, demonstrating the efficacy, safety, tolerability and convenience of roxadustat in patients with anaemia of CKD. Trials have been conducted in patients who are non-dialysis dependent, and those who are on dialysis The roxadustat evidence from the clinical trial programme addresses the need for an effective, generally well tolerated, oral treatment	Comments noted. No action required.
Wording	Astellas	Slightly amended wording of the remit: “To appraise the clinical and cost effectiveness of roxadustat within its marketing authorisation for treating anaemia in adult patients with chronic kidney disease.” Slightly amended wording of the title of the appraisal:	Comments noted. Following the consultation and scoping workshop, the scope title and remit have been updated to specify adults. Please see responses to the population consultation comments.

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		"Roxadustat for treating anaemia in adult patients with chronic kidney disease ID1483"	
Timing Issues	Astellas	Marketing authorisation is expected in [redacted] (CHMP [redacted]	Comments noted. No action required.
	Anaemia Nurse Specialist Association	Given that treatments pre-exist to treat anaemia in CKD there is not a relative urgency for proposed appraisal	Comments noted. No action required.

Comment 2: the draft scope

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Background information	Anaemia Nurse Specialist Association	Accuracy and completeness of information is wholly correct, relevant and precise	Comments noted. No action required.
The technology/ intervention	Astellas	Changes in the description of the technology that Astellas would like to request are: Insert the brand name for roxadustat, which is EVRENZO™ Amend paragraph 1: "Roxadustat activates the oxygen-sensing HIF pathway, mimicking the body's normal response to hypoxia. More specifically, roxadustat binds to prolyl hydroxylase enzymes preventing the breakdown of hypoxia-inducible factor alpha (HIFα). This in turn allows for dimerisation with the HIFβ unit and the resultant complex can bind to hypoxia response elements on multiple genes, including genes that regulate EPO production. Stimulation of these genes via the inhibition of HIF-PH leads to erythropoietin production, which in turn causes erythropoiesis and can also lead to increased iron uptake by	Comments noted. The technology section is designed to give a brief overview of the mechanism only. Further information about the mechanism of action can be presented in the company submission. The scope has been updated to include information about

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		reducing the expression of the peptide hormone hepcidin, which regulates the absorption of iron into the bloodstream. Roxadustat is administered orally." Amend the latter part of paragraph 2 where the trials are described to confirm the number, their respective patient populations and comparators: "Roxadustat has been studied in eight international Randomised Control Trials (RCTs). Four of these RCTs 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 (darbopoetin), and in three the comparator was placebo. In the remaining four RCTs the participants had end-stage renal disease and were receiving dialysis, and the comparator was ESA therapy."	the clinical evidence base for clarity.
	Anaemia Nurse Specialist Association	The technology intervention reads as an accurate account.	Comment noted. No action required.
Population	Astellas	Slight amended wording: "Adult patients with anaemia of CKD." Astellas considers there are two relevant populations to consider – those who are non-dialysis dependent, and those who are on dialysis	Comment noted. An adult population has been specified in the updated scope. The population has been kept broad in the scope. The company can put forward the case forward for any sub-groups in their submission.
	The Renal Association	Yes; if available data permits then non haemodialysis CKD and those patients on haemodialysis should be considered separately.	Comment noted. The population has been kept broad in the scope. The

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			company can put forward the case for any sub-groups in their submission.
	Anaemia Nurse Specialist Association	Given the potential for blood loss in the haemodialysis population this group should be considered separately.	Comment noted. The population has been kept broad in the scope. The company can put forward the case for any sub-groups in their submission.
Comparators	Astellas	Current "best alternative care" is erythropoiesis stimulating agents (ESAs) with or without concomitant iron therapy (oral or IV) ESAs are the relevant comparator, with darbopoetin the most widely used in England and Wales, although ESAs are clinically similar in terms of efficacy, safety, tolerability and convenience IV iron is not a comparator per se because it is an adjunctive therapy	Comment noted.The scope has been updated to specify ESAs, in line with the discussion at the scoping workshop.
	Anaemia Nurse Specialist Association	Comparisons should be made to other HIF stabilisers.	Comment noted. The remit of this appraisal is to compare roxadustat with current clinical management.
Outcomes	Astellas	The outcomes listed in the draft scope are relevant. Astellas would suggest also adding the following: ➢ Use of concomitant iron therapy in patients already on treatment with an ESA	Comment noted. In the updated scope, the use of rescue therapy outcome now specifies use of additional therapies including iron therapy for both the intervention and comparator. Mortality has been added as

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			an additional outcome, as discussed in the scoping workshop.
Economic analysis	Astellas	Anaemia of chronic kidney disease is a chronic condition. In order to capture all the relevant costs and health outcomes associated with roxadustat and its comparators, Astellas considers a lifetime horizon to be appropriate in the economic analysis Erythropoiesis stimulating agents (ESAs) are currently tendered in England and Wales, with net prices varying. Given tenders are informal agreements that can be withdrawn by the manufacturers at any time, Astellas proposes to use the list price for ESAs in the base case economic analysis. Astellas further proposes to test different pricing options in the sensitivity analyses	Comment noted. No action required.
	The Renal Association	Up to 5 – 10 years would be an appropriate horizon if possible	Comment noted. No action required.
	Anaemia Nurse Specialist Association	Seems entirely reasonable to determine cost effectiveness in terms of incremental cost per quality adjusted life year	Comment noted. No action required.
Equality	Astellas	Astellas is not aware of any issues of equality in the management of anaemia of chronic kidney disease in England and Wales	Comment noted. No action required.
	Anaemia Nurse Specialist Association	I find the proposed scope and remit to be justifiable and equitable.	Comment noted. No action required.
Innovation	Astellas	Astellas considers that roxadustat represents an innovative technology	Comment noted. The extent to which the technology may

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		Roxadustat represents an effective treatment approach, for patients who are non-dialysis dependent, and those who are on dialysis, or where an oral approach is a benefit to the patient or the service Roxadustat is a first in class medicine. Its mechanism of action functions at the level of the cellular oxygen sensing pathway in the body. The work on the mechanisms of oxygen sensing and the role of HIF won the Nobel Prize in Physiology / Medicine for 2019	or may not be innovative will be considered in any appraisal of the technology. No action required.
	The Renal Association	Yes; obviously this drug allows oral therapy for renal anaemia, so it may be a step change in certain circumstances. However, it will increase pill burden in a population taking multiple pills; for the haemodialysis patient they may prefer having an intravenous injection on dialysis (when intravenous access already happens) rather than take another pill.	Comment noted. The extent to which the technology may or may not be innovative will be considered in any appraisal of the technology. No action required.
	Anaemia Nurse Specialist Association	Yes given the complexities with the incidence of infection and inflammation in the CKD population resulting in iron deficient anaemia this technology is set to revolutionise anaemia management and improve health outcomes and will substantially improve quality of life.	Comment noted. The extent to which the technology may or may not be innovative will be considered in any appraisal of the technology. No action required.
Questions for consultation	Astellas	**Is the population defined appropriately?** ➢ Slight amend to “Adult patients with anaemia of CKD.” **Is roxadustat a suitable treatment for patients who are iron deficient? Would patients be offered roxadustat in conjunction with iron therapy?**	Comments noted. Changes to the scope as previously stated.

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		➢ Roxadustat could be a suitable treatment for patients who are iron deficient depending on the degree of iron deficiency ➢ Patients would continue oral and/or IV iron, with the potential for the dose or frequency to be reduced, when being treated with roxadustat **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?** ➢ Current "best alternative care" is erythropoiesis stimulating agents (ESAs) with or without concomitant iron therapy (oral or IV), which is allowed for in the scope ➢ Darbopoetin is the most widely used ESA in England and Wales in this population ➢ IV iron should not be considered a comparator as it is an adjunctive therapy **Are the outcomes listed appropriate? Are there any other key clinical or patient outcomes that should be included?** ➢ The outcomes listed in the draft scope are relevant. ➢ Astellas would suggest also adding the following: o Use of concomitant iron therapy in patients already on treatment with an ESA **Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom roxadustat is**	

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		expected to be more clinically effective and cost effective or other groups that should be examined separately? ➢ It is relevant to consider roxadustat in patients who are non-dialysis dependent, and those who are on dialysis **Where do you consider roxadustat will fit into the existing NICE pathway Anaemia management in people with chronic kidney disease overview (2017)?** ➢ Roxadustat should be considered within its anticipated licensed indication ➢ Astellas believes that roxadustat will fit into the space serviced by erythropoiesis stimulating agents (ESAs) in the current treatment pathway **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;**	

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		• **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.** ➢ Astellas is not aware of any issues with this regard **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)?** ➢ Astellas considers that roxadustat represents an innovative technology ➢ Roxadustat represents an effective treatment approach, for patients who are non-dialysis dependent, and those who are on dialysis, or where an oral approach is a benefit to the patient or the service ➢ Roxadustat is a first in class medicine. Its mechanism of action functions at the level of the cellular oxygen sensing pathway in the body. The work on the mechanisms of oxygen sensing and the role of HIF won the Nobel Prize in Physiology / Medicine for 2019 **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?**	

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		➢ Astellas believes that the benefit offered to patients in having a novel, oral treatment in this space is unlikely to be captured adequately by the EQ-5D ➢ This is of particular relevance for non-dialysis patients for whom the availability of such a treatment option may result in fewer visits into hospital, and a consequently reduced disruption to normal life. Additionally it may lead to a reduced impact and reliance on home care for administration of treatment ➢ In addition, roxadustat provides an alternative for those patients who have a phobia of needles or are unable to self-inject **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** ➢ Additional evidence about the benefit of such an oral approach is to be captured in a patient preference study, and Astellas intends to look for supportive evidence in the literature **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.** ➢ Astellas is not aware of any major barriers **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).**	

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		➢ Astellas agrees with this approach	