Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

Surrey Downs, Guildford & Waverley, North West Surrey, East Surrey Place & associated partner organisations

NICE Technology Appraisals: Local implementation

NICE TA Guidance name and number	Roxadustat for treating symptomatic anaemia in chronic kidney disease TA807		
Available at	https://www.nice.org.uk/guidance/ta807		
Date of issue	13 July 2022	**Implementation deadline**	13 October 2022

Medicine details[1,2]	
Name, brand name and manufacturer	Roxadustat (Evrenzo®, Astellas Pharma)
Mode of action	Roxadustat is a hypoxia-inducible factor, prolyl hydroxylase inhibitor (HIF-PHI), which stimulates a coordinated erythropoietic response, thereby increasing haemoglobin production and improving iron bioavailability.
Licensed indication	Roxadustat is indicated for treatment of adult patients with symptomatic anaemia associated with chronic kidney disease (CKD).
Formulation	20mg,50mg,70mg,100mg and 150mg film-coated tablets
Usual dosage	The appropriate dose of roxadustat must be taken orally three times per week and not on consecutive days. The dose should be individualised to achieve and maintain target Hb levels of 10 to 12 g/dL. Roxadustat treatment should not be continued beyond 24 weeks of therapy if a clinically meaningful increase in Hb levels is not achieved. Alternative explanations for an inadequate response should be sought and treated before re-starting Evrenzo. Please see the section 4.2 of the SmPC at: https://www.medicines.org.uk/emc/product/12835 for further details of starting dose at treatment initiation, dose adjustment and haemoglobin monitoring and maintenance dose.
Comparison with NICE TA use[3]	The NICE TA recommendations are tighter than the SmPC. SmPC: Roxadustat is indicated for treatment of adult patients with symptomatic anaemia associated with chronic kidney disease (CKD). NICE TA: they have *stage 3 to 5 CKD* with *no iron deficiency* and they are *not* on dialysis at the start of treatment *This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and **will not be routinely funded** by local commissioners.*

Disease and potential patient group	
Brief description of disease[3]	Anaemia is a serious condition defined by abnormally low levels of haemoglobin (Hb) or too few red blood cells in the blood. This reduces the ability of blood to carry oxygen around the body. Erythropoietin, a hormone produced by the kidneys in response to low oxygen levels, stimulates the bone marrow to produce red blood cells. However, kidneys that are not working properly make less erythropoietin, so anaemia is common in people with chronic kidney disease (CKD). CKD is characterised by the progressive loss of kidney function and is generally categorised into 5 stages based on decreasing kidney function. The prevalence and severity of anaemia increase as kidney disease worsens (6% of people with stage 1 CKD have anaemia compared with 34% and 43% of people with stage 4 and 5 CKD, respectively). People with CKD already face substantial challenges that affect their quality of life. Symptoms of CKD include fatigue, itching, swelling and sleep problems. These can affect many aspects of normal life and people's capacity to stay in work. Also, people with CKD experience stress and difficulties coming to terms with the diagnosis of an incurable, progressive disease and making difficult decisions about treatment, including dialysis. Anaemia further affects their quality of life. The patient expert explained that the symptoms of untreated anaemia are severe and disabling. For example, some people cannot drive, work, or even walk because of the extreme fatigue associated with anaemia. As a result, this can affect mental health. The patient expert added that people going into dialysis need relief from anaemia-associated fatigue to make decisions about their treatment and manage their life around dialysis. The committee concluded that anaemia can be associated with extreme fatigue and has a considerable effect on quality of life for people with CKD.
Potential patient numbers per 100,000	See appendix 1 - Appendix 97/100,000

SUMMARY

Guidance[2]
Recommendations 1.1 Roxadustat is recommended as an option for treating symptomatic anaemia associated with chronic kidney disease (CKD) in adults only if: • they have stage 3 to 5 CKD with no iron deficiency and • they are not* on dialysis at the start of treatment and • the company provides roxadustat according to the commercial arrangement. 1.2 This recommendation is not intended to affect treatment with roxadustat that was started in the NHS before this guidance was published. People having treatment outside this

recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Please note:
**Current treatment is with erythropoiesis stimulating agents (ESAs), which are injectable analogues of erythropoietin that can be given subcutaneously, intravenously, or through the haemodialysis machine.*

Experts confirmed that because intravenous iron and some ESAs are administered through the dialysis machine, the main benefit of roxadustat as an oral treatment would be for treating anaemia in people not on dialysis.

Why the committee made these recommendations

Treatment for symptomatic anaemia associated with chronic kidney disease includes erythropoiesis stimulating agents (ESAs). Roxadustat is an alternative to ESAs.

A clinical trial comparing roxadustat with darbepoetin alfa (an ESA) shows that roxadustat works as well as darbepoetin alfa.

The cost effectiveness estimates for roxadustat are within what NICE normally considers an acceptable use of NHS resources. So roxadustat is recommended.

Other factors e.g. equality issues

There are no equality issues relevant to the recommendations.

Cost implications* [2,3,4]

Cost:
Annual or monthly cost per patient:
The list prices of roxadustat are (excluding VAT; BNF online, accessed December 2021) per 12-tablet pack:

Strength	Price per 12-tablet pack (monthly cost)	Annual cost (13 packs)
20 mg	£59.24	£770.12
50 mg	£148.11	£1,925.43
70 mg	£207.35	£2,695.55
100 mg	£296.21	£3,850.73
150 mg	£444.32	£5,776.16

The company has a commercial arrangement. This makes roxadustat available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Has dose escalation been considered as part of the NICE costing template?
The dose should be individualised to achieve and maintain target Hb levels of 10 to 12 g/dL.

Costing information per CCG:

1. NICE resource impact statement*

Table 1: The estimated number of people in England and NHS Surrey Heartlands ICS receiving roxadustat using NICE assumptions 2022/23 and 2026/27 (see appendix 1 - Appendix).

Estimated number of people	2022/23	2026/27
Uptake rate for roxadustat (%)	8	22
Population in England receiving roxadustat each year	3,500	9,800
Population in Surrey Heartlands ICS receiving roxadustat each year	66	181

2. **NICE resource impact template**

Table 2a: The change of total drugs cost per year over 5 years, starting 2022/23 for Surrey Heartlands ICS.

	Change in costs £'000				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Surrey Heartlands ICS	-£22	-£54	-£62	-£62	-£63

Table 2b: Impact of activity change on costs over 5-year period starting 2022/23 for Surrey Heartlands ICS at year 5.

Drug costs	Activity change	Impact of change on cost at year 5
Proportion of people who choose roxadustat	181	£131,767
Proportion of people who choose epoetin alfa	-9	-£19,225
Proportion of people who choose darbepoetin alfa	-147	-£155,358
Proportion of people who choose epoetin beta	-9	-£15,838
Proportion of people who choose epoetin zeta	-9	-£4,172
Proportion of people who choose methoxy polyethylene glycol-epoetin beta	-7	-£570
Drug costs - total resource impact	0	**-£63,395**

This predicts a negative impact on costs of -£63,395 at year 5, given the limitations of the resource impact template which predicts the same number of patients in 5 years' time (assuming homecare services are started and there are no charges for homecare costs).

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

Availability of PAS and details (if appropriate):
Yes – a commercial arrangement which makes roxadustat available to the NHS with a discount.

The commercial arrangement only applies to trusts and primary care services would not be able to prescribe and supply at this reduced price, in line with the NICE TA.

Availability of homecare service (if appropriate): Yes

Alternative treatments and cost per patient per year

Other NICE recommended products:
Roxadustat is a first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor, which provides an additional treatment for anaemia associated with CKD.

Options not reviewed by NICE but used in standard practice:
ESAs are:

- epoetin alfa
- darbepoetin alfa
- epoetin beta
- epoetin zeta
- methoxy polyethylene glycol-epoetin beta

Impact to patients

- An additional treatment option would be valued by patients.
- Anaemia associated with CKD may be treated with iron therapy, erythropoiesis stimulating agents (ESAs), or both. Current ESAs are injectable analogues of erythropoietin that can be given subcutaneously, intravenously, or through the haemodialysis machine and ESAs are typically self-administered. Roxadustat is an oral treatment, which would be valued, particularly those who find it difficult to self-inject.
- This medicine is available under a homecare service so will be delivered directly to the patient (as are ESAs).
- All the existing therapies are administered via subcutaneous injection so use of roxadustat reduces waste from device use and is more convenient and easier for patients.

Impact to primary care prescribers

- This is a National Tariff excluded high-cost drug and is commissioned by integrated care systems (ICS) / clinical commissioning groups (CCG) for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Impact to secondary care

- Providers are NHS hospital trusts.
- The initiation, administration and on-going treatment is managed by secondary care.
- Homecare arrangements will be managed by the trust. Currently ESAs are also managed by the homecare so this would be instead of an ESA.
- An additional treatment option would be valued by clinicians.

Impact to commissioners

- The technology is commissioned by ICSs and they are required to comply with the recommendations in a NICE TA within 3 months of its date of publication.
- Having an oral alternative might reduce costs associated with ESA administration and reduce the need for cold-chain storage and special sharps disposals. Roxadustat might also simplify management of anaemia by reducing the need for iron transfusions.
- As the dose should be individualised to achieve and maintain target Hb levels of 10 to 12 g/dL, it is difficult to predict costs.

Implementation

- NICE TA implementation must be within 90 days of publication.
- Blueteq forms to be developed.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- The company in its submission added that roxadustat would only be offered to people

who are not on dialysis (including peritoneal dialysis), but people starting roxadustat would be able to continue treatment if they went on to dialysis.

Recommendation to APC

National Tariff excluded high-cost drug: Yes

Recommended traffic light status: RED

Additional comments:
The committee noted that roxadustat is a first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor, which provides an additional treatment for anaemia associated with CKD. However, it was aware that roxadustat was shown only to be non-inferior to current treatment. The patient expert indicated that roxadustat's oral administration is a step-change compared with injectable ESAs, even though this might affect whether people will take roxadustat as intended. Having an oral alternative might reduce costs associated with ESA administration and reduce the need for cold-chain storage and special sharps disposals. Roxadustat might also simplify management of anaemia by reducing the need for iron transfusions. The committee recalled that the company already included fewer iron infusions and costs of ESA administration costs in its economic model. So, the committee concluded that roxadustat did not meet NICE's criteria to be considered an innovative treatment.

References:

1 Specification of Product Characteristics. emc. Available at: https://www.medicines.org.uk/emc/product/12835 Accessed 1.8.22

2 Drug action. BNF NICE. Available at: https://bnf.nice.org.uk/drugs/roxadustat/ Accessed 1.8.22

3 NICE Technology Appraisal Guidance. Roxadustat for treating symptomatic anaemia in chronic kidney disease. Technology appraisal guidance [TA807] Published: 13 July 2022. Available at https://www.nice.org.uk/guidance/ta807 Accessed 1.8.22

4 NICE Resource impact report: Roxadustat for treating symptomatic anaemia in chronic kidney disease. Technology appraisal guidance [TA807] Published: 13 July 2022 . Available at: https://www.nice.org.uk/guidance/ta807/resources Accessed 1.8.22

5 NICE Resource Impact template: Roxadustat for treating symptomatic anaemia in chronic kidney disease. Technology appraisal guidance [TA807] Published: 13 July 2022 . Available at: https://www.nice.org.uk/guidance/ta807/resources Accessed 1.8.22

Declaration of interest:

Appendix 1: Number of people eligible for treatment in England and NHS Surrey Heartlands ICS Population[4,5]

	Proportion of previous row (%)	Number of people in 2026/27 England	Number of people in 2026/27 NHS Surrey Heartlands ICS
Adult population		46,263,200	851,080
Prevalence of chronic kidney disease stage 3-5	6.76	3,127,392	57,533
Proportion of people who are non-dialysis dependant	99.05	3,097,682	56,986
Proportion of people who are undergoing treatment in secondary care	6.75	209,094	3,847
Proportion of people who have anaemia[1]	35.66	74,563	1,372
Total number of people eligible for treatment with roxadustat	60.0	44,738	823
Total number of people estimated to receive roxadustat in 2022/23	8.0	3,579	66
Total number of people estimated to receive roxadustat each year-by-year 2026/27 based on predicted population growth	22.0	9,800	181