National Institute for Health and Care Excellence

Health Technology Evaluation

Single Technology Evaluation
Daprodustat for treating anaemia in adults with chronic kidney disease ID3987

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	GSK	GSK considers that it is appropriate for daprodustat to be referred to NICE for appraisal.	Comment noted, no action required.
Wording	GSK	The wording of the remit reflects the draft scope.	Comment noted, no action required.
Additional comments on the draft remit	GSK	GSK aims to progress the submission for daprodustat in line with NICE timelines.	Comment noted, no action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GSK	**Background - Paragraph 1 Symptoms associated with anaemia of CKD** GSK requests that the word 'Possible' is deleted from the last sentence, as these commonly reported adverse effects of anaemia of chronic kidney disease (CKD) are well recognised. GSK also request that the following symptoms related to anaemia of CKD, are also included. • Fatigue is recognised as one of the most commonly reported symptoms of anaemia of CKD which is associated with considerable detrimental impact on quality of life of people with anaemia of CKD and should be included.[1] • Other commonly reported symptoms with detrimental impact on patient quality of life i.e. feeling weak, forgetfulness, impaired concentration, shortness of breath, decreased physical activity and depression should also be noted in this paragraph.[1] **Requested insertion – after paragraph 2** GSK considers it important that the additional burden imposed by anaemia of CKD on people's quality of life, over and above that experienced by people with CKD alone, should be emphasised in the background information. Up to 95% of people with anaemia of CKD believe that their daily life is affected by symptoms of anaemia, particularly fatigue.[1] In a cross-sectional European study, people with anaemia of CKD reported lower EQ-5D scores than those at an equivalent CKD stage without anaemia.[2] Anaemia of CKD can also have considerable impact on people's mental health and wellbeing. In a study of people with anaemia of CKD from five European countries (n=203 total; n=67 from the UK), 80% of participants reported feeling emotionally affected by their disease, and 37% (39% for UK participants)	Comment noted. The word 'Possible' has been removed. Fatigue has been added to the scope. It is noted that some of the other commonly reported adverse events are already in the scope. It is intended that the background to the scope gives a brief overview of the condition. It is anticipated that the impact of the condition on people's quality of life and daily activities will be discussed in the appraisal. No further updates have been made to the scope.

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		experienced a negative impact on their mental health secondary to anaemia of CKD.[3]	
Technology	GSK	**First line amendment:** Please note the proposed proprietary name for daprodustat in the UK is (Jesduvroq®). **Paragraph 2** **Daprodustat clinical trial programme** The description of the daprodustat trial programme in the draft scope does not fully describe the evidence base supporting this therapy; GSK requests this section is expanded with the following wording. The comprehensive trial programme included two pivotal, Phase III, trials that compared daprodustat with erythropoiesis-stimulating agents (ESAs) in almost 7000 people with anaemia of CKD who were not on dialysis (ASCEND-ND) and who were on dialysis (ASCEND-D). Median follow-up was 2.5 years in ASCEND-ND and 1.9 years in ASCEND-D. The ASCEND-ND study included participants who transitioned to dialysis during the study and remained in the study when they made this transition and therefore included incident dialysis participants. These studies also included people switching from ESA therapy to daprodustat or who were ESA-naïve. Three smaller, Phase III studies, of a shorter duration confirmed the starting dose in incident dialysis participants with limited or no prior ESA therapy (ASCEND-ID, N=312), confirmed the doses of daprodustat for thrice weekly therapy in dialysis participants (ASCEND-TD, N=407), and demonstrated	Comments noted. The brand name has been updated in the scope. Comments noted. This section is intended to give a brief overview of trial data. No action required.

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		efficacy and quality of life relative to placebo in non-dialysis participants (ASCEND-NHQ, N=614).'[4-8]	
Population	GSK	The draft scope is accurate, no amendments are required.	Comment noted, no action required.
	Astellas	Astellas suggests that the population should be defined as being specific to chronic kidney disease (CKD) stages 3-5. The NICE Clinical Guideline for CKD (NG203) recommends patients are referred into secondary care for treatment of anaemia associated with CKD from stage 3 onwards, with the comparator treatments prescribed in secondary care only. CKD stages 3-5 also align to the population included in the clinical trials for this disease area. Furthermore, it is suggested that the population should refer to 'symptomatic' anaemia as NG203 suggests to offer treatment for anaemia associated with CKD to patients who are likely to benefit in terms of quality of life and physical function.	Comment noted, The population is kept broad in the scope. Daprodustat will be appraised within its marketing authorisation. No changes needed to the scope.
Comparators	GSK	**Positioning of daprodustat in the treatment pathway** Daprodustat will offer people with anaemia of CKD an alternative option to ESAs after, and in conjunction with, iron therapy. **Relevance of roxadustat as a comparator** Daprodustat is supported by a body of evidence across a continuum of anaemia of CKD as described above. GSK considers that roxadustat should	Comments noted. Roxadustat has been included subject to ongoing appraisal. This is to allow for the possibility of roxadustat having a NICE

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		not be included as a relevant comparator for this submission for the reasons outlined below. **Departure from the NICE methods guidde** The NICE methods guide states comparators should include treatments that are "established practice in the NHS".[9] Roxadustat has not yet been recommended for use in UK clinical practice and therefore, cannot be considered to represent a treatment that is established practice in the NHS for people with anaemia of CKD.	recommendation and being in established practice at the time of the appraisal of daprodustat. Should roxadustat not have a NICE technology appraisal recommendation it will no longer be a potential comparator. No updates to the scope needed.
Outcomes	GSK	The draft scope is accurate, no amendments are required.	Comment noted, no action required.
Equality	GSK	**The draft scope excluded the population who are not able to take ESAs. GSK's target population for daprodustat promotes equality by widening the population with anaemia of CKD who would be eligible for treatment.**	Comments noted. The population does not exclude people who cannot take ESAs. However it is noted that there was no comparator listed in the draft scope for people who cannot have ESAs. Therefore a broad comparator of established clinical

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			practice without erythropoiesis stimulating agents has been added to the comparator section of the scope.
Other considerations	GSK	**Oral administration** The oral administration method of daprodustat can avoid the injection-site reactions and injection burden on people with anaemia of CKD compared to intravenous (IV) / subcutaneous (SC) ESAs. Convenience associated with daprodustat Daprodustat can be administered across a broad adult patient population, allowing for treatment transition upon progression from being non-dialysis-dependent to incident-dialysis to being dialysis-dependent across different modalities of dialysis, reflecting the patient journey in clinical practice.[4-8] Daprodustat provides a convenient oral dosing regimen, including both once daily (in non-dialysis-dependent) and three times weekly (in dialysis-dependent) dosing options, and varying dose strengths. Dosing can therefore be aligned for people with anaemia of CKD and physician needs, with dose titration allowing for a controlled rise in Hgb levels for individualised care.[4-8] Daprodustat, as an oral therapy, has a number of potential advantages versus IV/SC ESAs, as it is more easily delivered, stored and administered, reducing clinical resource use (including nurse training and administration times). Daprodustat does not require cold-chain storage and transit or refrigeration in the patient's home, and is also associated with fewer additional considerations related with disposal in comparison to ESAs (for	Comments noted. No action required.

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		example, once syringes are used, they become biohazard material and require specific ways of disposal and destruction).[4-8] Accordingly, daprodustat is expected to be associated with cost and resource use savings for the NHS relative to ESAs.	
Questions for consultation	GSK	**Positioning of daprodustat in the treatment pathway** Daprodustat is anticipated to be an alternative to ESAs in the patient pathway, after and in conjunction with iron therapy. **ESAs considered to be most used** ESAs, listed in the British National Formulary, will be considered as relevant comparators, and will be modelled as a class assuming equivalent efficacy of treatment across the different types of ESAs. **Clinical and cost effectiveness of daprodustat in sub-groups** It is not possible to respond robustly to this question at this stage of the process. Sub-groups will be explored. **Benefits not captured in the QALY calculation** The ability to perform dose titration with daprodustat to achieve optimal patient Hb within the target ranges will be a benefit that will not be included in the QALY calculations. In addition, the benefit in having an oral treatment with a novel mode of action, with the resulting convenience of administration, is unlikely to be captured adequately by the EQ-5D, and subsequently, the QALY calculations. This is of particular relevance in non-dialysis where the	Comments noted. No action required.

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		availability of such a treatment option may result in fewer visits to hospital, and consequently a reduced disruption to normal life. It is unlikely that all of the cost and resource use savings resulting from daprodustat not needing refrigeration, nurse time for administration, sharp or biohazard disposals, as well as the potentially longer in-use shelf life of daprodustat relative to ESAs, will be fully captured in the QALY calculation. Additionally, the method of oral administration may lead to a reduced impact and reliance on nurse/carer resource for administration of treatment in the home.	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

none