National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Tivozanib for treating renal cell carcinoma

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	EUSA PHARMA	Planned indications: [redacted]	Comment noted. The scope has been amended to reflect this.
Wording	Novartis	Yes [the wording is acceptable]	Comment noted.
	EUSA PHARMA	Wording acceptable	Comment noted.
	NCRI-ACP-RCP-RCR	Yes [the wording is acceptable]	Comment noted.
Timing Issues	Novartis	Little urgency	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	EUSA PHARMA	We believe that the appraisal is urgent to the NHS due the potential to provide a more cost effective alternative to the currently available targeted therapies in Renal Cell Carcinoma.	Comment noted.
	NCRI-ACP-RCP-RCR	Drugs already NICE approved in 1st and 2nd line setting in metastatic renal cell carcinoma (mRCC), therefore relative urgency is less than if this had not been the case.	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novartis	Since the draft scope was written nivolumab has been NICE approved and cabozantinib and lenvatinib + everolimus are also undergoing NICE appraisals for use in second line.	Comment noted. The background section has been altered to reflect the publication of NICE technology appraisal guidance 417.
	EUSA PHARMA	Background information is accurate and complete	Comment noted.
	NCRI-ACP-RCP-RCR	Update required regarding positive outcome from NICE technology appraisal for Nivolumab in mRCC (ID853).	Comment noted. The background section has been altered to reflect the publication of NICE technology appraisal guidance 417.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention	Novartis	It would be good to include further detail of the clinical trials that are reported, e.g. NCT numbers, trial status.	Comment noted. It is not standard practice for NICE to report trial names and numbers in scoping documents.
	EUSA PHARMA	In the second paragraph of this section there are some inaccuracies. a) The first study cited (tivozanib vs sorafenib in patients with untreated disease or 1 prior systemic treatment) has been completed and is published. b) Although the second study cited (tivozanib vs sorafenib in patients with 2-3 previous failed treatments) is currently recruiting, its estimated completion date is October 2018 and it will consequently be of no relevance to this appraisal.	Comment noted. The reference to the trial has been retained for completeness.
	NCRI-ACP-RCP-RCR	Yes, although details are lacking/awaited on the outcome of ongoing studies.	Comment noted.
Population	Novartis	Further definition on which line of therapy tivozanib is to be appraised is required. Trial data relates to clear cell RCC only.	Comment noted. The population has been defined to reflect the population enrolled into the clinical trials and who could potentially be included within the marketing authorisation
	EUSA PHARMA	[redacted]	Comment noted. The population has been defined to reflect the population enrolled into

Section	Consultee/ Commentator	Comments [sic]	Action
		[redacted]	the clinical trials and who could potentially be included within the marketing authorisation.
	NCRI-ACP-RCP-RCR	Yes [it is appropriate]	Comment noted.
Comparators	Novartis	Yes [the comparators are relevant]	Comment noted.
	Pfizer	Pfizer notes that there is an ongoing NICE appraisal of cabozantinib for people with previously treated renal cell carcinoma, and therefore, if timelines permit, and it is appropriate to assess tivozanib in people with previously treated recurrent or metastatic disease, Pfizer recommends that cabozantinib is also included as a comparator in this appraisal.	Comments noted. Cabozantinib has been added as a potential comparator.
	EUSA PHARMA	[redacted]	Comment noted. [redacted]

Section	Consultee/ Commentator	Comments [sic]	Action
		[redacted]	[redacted] Therefore, the scope has not been changed.
	NCRI-ACP-RCP-RCR	Yes [it is appropriate]	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	EUSA PHARMA	Yes [they are appropriate]	Comment noted.
	NCRI-ACP-RCP-RCR	Yes [they are appropriate]	Comment noted.
Economic analysis	EUSA PHARMA	Survival duration in advanced renal cell carcinoma is relatively limited, with a median overall survival duration of around 3 years. Individual patients, however, may survive for considerably longer, perhaps up to 10 years. We consequently believe that a lifetime horizon is the most appropriate one to use in this case.	Comment noted. NICE's 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.
Equality and Diversity	EUSA PHARMA	We do not believe the proposed remit needs to change from the perspective of equality.	Comment noted.
	NCRI-ACP-RCP-RCR	None identified	Comment noted.
Innovation	Novartis	The technology is not considered as a 'step-change' in the management of this condition. The use of the technology will not result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation.	Comments noted. The potential innovative nature of the technology will be considered by the appraisal committee.

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	NCRI-ACP-RCP-RCR	Tivozanib is an oral VEGF inhibitor used in the setting of mRCC. Whilst data is awaited from ongoing clinical studies, previous studies have demonstrated that it has efficacy and a manageable toxicity profile in this setting. Several other oral VEGF inhibitors (pazopanib, sunitinib, axitinib) are already established in clinical practice in this setting in England. Therefore, whether tivozanib represents a sufficient step change in terms of favourable efficacy and toxicity profile to make a substantial impact on health-related benefits is considered uncertain.	Comments noted. The potential innovative nature of the technology will be considered by the appraisal committee.
Questions for consultation	Novartis	Need to understand when results from NCT02627963 will be made available.	Comments noted. Information on trials can be obtained from publically available trial databases.
	NCRI-ACP-RCP-RCR	Marketing Authorisation for tivozanib is awaited and this will define where it fits in the existing NICE pathway for renal cancer, in particular which line of treatment it is considered for.	Comment noted.

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

Roche
Department of Health