National Institute for Health and Care Excellence

Health Technology Evaluation

Avelumab with axitinib for untreated advanced renal cell carcinoma (MA review of TA645) [ID6294]
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	Action Kidney Cancer	We consider this appraisal as appropriate for previously untreated advanced RCC.	Thank you for your comment. No action required.
	British Uro-oncology Group	The combination of IO/TKI's have shown to improve outcomes in patients with mRCC. This combination (Axi/Avelumab) has been approved for use by NICE via the CDF (TA 645). Agree with the evaluation route proposed.	Thank you for your comment. No action required.
Wording	Action Kidney Cancer	The wording of the remit needs to make it clear that there is an unmet need for an effective first-line treatment for people with previously untreated advanced/metastatic papillary, chromophobe, collecting duct and other rare subtypes of RCC, including sarcomatoid and rhabdoid features. The wording of the remit also needs to mention the inequity in access to RCC therapies between England and Scotland. Also, mention the fact that due to the heterogenous nature of RCC, patients need access to a choice of	Thank you for your comment. The appraisal committee will take into consideration the unmet need for an effective first-line treatment for people with RCC, including any relevant subgroups. The remit of

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		treatment options in the first line to enable a more individualised treatment plan.	the scope has been kept broad. No action required.
	British Uro-oncology Group	Yes	Thank you for your comment.
Timing Issues	Action Kidney Cancer	Relatively high urgency to level up access to treatments between England and Scotland to reduce inequalities in the first line setting.	Thank you for your comment. NICE will evaluate the technology within its marketing authorisation and has scheduled this topic into its work programme. For more information, please see https://www.nice.org.uk/guidance/awaiting-development/gid-ta11587

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Merck	The background information is accurate and comprehensive.	Thank you for your comment. No action required.

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	MSD	The background section currently contains the text: “TA858 recommends lenvatinib with pembrolizumab (a PD-1/PD-L1 inhibitor with a TKI) as an option…” However, as lenvatinib is the TKI and pembrolizumab is the PD-1/PD-L1 inhibitor, it is more correct and less likely to cause unnecessary confusion if this text is changed to: “TA858 recommends lenvatinib with pembrolizumab (a TKI with a PD-1/PD-L1 inhibitor) as an option…”	Thank you for your comment. The background section has been updated to reflect suggested change : “TA858 recommends lenvatinib with pembrolizumab (a TKI with a PD-1/PD-L1 inhibitor) as an option…”.
Population	Action Kidney Cancer	The population is defined appropriately	Thank you for your comment. No action required.
	British Uro-oncology Group	Yes	Thank you for your comment.
Subgroups	Merck	We recommend the addition of the favourable risk group for the following reasons: • Firstly, we would like to better reflect the current treatment landscape which is now fragmented into subgroups based on the International Metastatic RCC Database Consortium (IMDC) criteria. Secondly, we would like to align with anticipated NHS clinical practice as we have received feedback from clinical experts that the greatest unmet need and anticipated positioning for avelumab with axtinib in this new treatment landscape would be in the favourable risk group.	Thank you for your comment. “Favourable-risk advanced metastatic RCC as defined in the IMDC criteria” has been added to the list of subgroups listed in the scope.

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	Ipsen	The primary endpoint of JAVELIN 101 trial to show superiority either on progression-free or overall survival in a subpopulation (that is, people with PD-L1 positive tumours). Will this appraisal examine the results of PD-L1 positive and PD-L1 negative tumours? Recent NICE appraisals e.g. TA964 and TA858 have insisted on examining results in the population divided in to favourable risk and intermediate/poor risk RCC populations. Will this be done in this appraisal for consistency?	Thank you for your comment. “Favourable risk advanced metastatic RCC as defined in the IMDC criteria” and “ PD-L1 status” have been added to the list of subgroups listed in the scope.
	British Uro-oncology Group	It has to be considered in the favourable risk group patients as well, in addition to the intermediate and poor risk groups. There is increasing evidence that immunotherapy has a role to play in the favourable risk group patients. Moreover, up to 40-50% patients do not get 2nd line therapy.	Thank you for your comment. “Favourable risk advanced metastatic RCC as defined in the IMDC criteria” has been added to the list of subgroups listed in the scope.
Comparators	Merck	Merck propose the following comparisons to be included in our evidence submission: Favourable risk disease as defined in the IMDC criteria: • Pazopanib • Sunitinib • Tivozanib	Thank you for your comments. The scope has been updated to reflect the comparators as per ‘Favourable risk disease’ and ‘Intermediate risk disease’ as defined in

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		Intermediate/poor risk disease as defined in the IMDC criteria: • Cabozatinib • Nivolumab with ipilimumab • Lenvatinib with pembrolizumab • Cabozatinib with nivolumab • Tivozanib • Sunitinib Pazopanib.	the IMDC criteria. 'Pazopanib', 'Sunitinib' and 'Tivozanib' have been added as comparators for the 'Intermediate risk disease'.
	British Uro-oncology Group	Pazopanib, Sunitinib, Tivozanib are appropriate comparators for favourable risk group patients. Cabo, Len/Pem, Cabo/Nivo/ Ipi/Nivo are appropriate comparators for intermediate and poor risk group patients.	Thank you for your comment. No action required.
Outcomes	Merck	All outcomes listed are appropriate.	Thank you for your comment. No action required.
	Action Kidney Cancer	Recommend adding identification of a prognostic/predictive biomarker.	Thank you for your comments. The list of outcomes is not exhaustive. Stakeholders can provide justification around the most appropriate outcomes and the committee will consider this during

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			the appraisal. No action required.
	British Uro-oncology Group	Yes	Thank you for your comment.
Equality	Action Kidney Cancer	Ensure there is good representation of people from BAME cultures and deprived areas of England and Wales. Ensure equity of access to avelumab/axitinib on the NHS regardless of where the patient lives. Ensure equity of access to avelumab/axitinib for people with all subtypes of RCC, including RCC with sarcomatoid and rhabdoid features. Ensure equity of access for people with RCC brain metastases.	Thank you for your comment. NICE appraises technologies within their licence. NICE welcomes input from stakeholders to give insight into clinical practice. The committee will make decisions based on the evidence presented by the submitting company. It will take into account evidence for specific groups, including race and subgroups for RCC, in its decision making.
	British Uro-oncology Group	No obvious discrimination is evident	Thank you for your comment. No action required.

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Questions for consultation	Merck	1. Where do you consider avelumab with axitinib will fit into the existing care pathway for renal cell carcinoma? Merck: We have received feedback from clinical experts that the greatest unmet need and anticipated positioning for avelumab with axtinib in this new treatment landscape would be in the favourable risk group. However, in line with its marketing authorisation, avelumab with axitinib can be considered as an option across all IMDC risk groups. 2. Please select from the following, will avelumab with axitinib be: A. Prescribed in primary care with routine follow-up in primary care / B. Prescribed in secondary care with routine follow-up in primary care/ C. Prescribed in secondary care with routine follow-up in secondary care/ D. Other (please give details): Merck response: C. Prescribed in secondary care with routine follow-up in secondary care. 3. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Merck response: No, the setting for prescribing and routine follow-up will be the same for comparators. 4. Do you consider that the use of avelumab with axitinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Merck response: No.	Thank you for your comment.
	Ipsen	Position in pathway: Option C: Like other IO/TKI therapies this treatment with be prescribed in secondary care with routine follow-up in secondary care.	Thank you for your comment.

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	Action Kidney Cancer	In NHS clinical practice, how will clinicians choose between the various first-line treatment options for individual patients? Will this be on IMDC criteria, radiographical evidence, pathology, patient characteristics and personal preference? We need to identify prognostic/predictive biomarkers for avelumab/axitinib treatment to enable clinicians to determine which RCC patients would benefit most from this treatment.	Thank you for your comment. The committee will consider during the appraisal whether there are subgroups that would benefit more from this treatment.
	British Uro-oncology Group	This combination will be prescribed in secondary care with routine follow-up in secondary care	Thank you for your comment.
Additional comments on the draft scope	MSD	In the Related NICE recommendations, Related technology appraisals section, it may be useful to also provide references to technology appraisals for NICE-recommended subsequent treatments that would be considered in cost-effectiveness analyses i.e. TA417 Nivolumab for previously treated advanced renal cell carcinoma.	Thank you for your comment. The population being evaluated in this appraisal, in line with the marketing authorisation for avelumab with axitinib, is untreated renal cell carcinoma. In line with the population for the scope, only technology appraisals related to untreated RCC are included. No action required.

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

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