National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy [ID3735]

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
Wording	Merck Serono Ltd	The wording of the remit reflects the issue(s) of clinical and cost-effectiveness about this technology.	Comment noted. No action required.
Timing Issues	Merck Serono Ltd	Patients with metastatic urothelial carcinoma who respond to platinum-based chemotherapy, often experience progression as response is not durable, which results in poor overall survival. Due to quick progression of the disease and performance status at this later line many patients do not receive 2nd line+ treatments, with the options available having limited clinical effectiveness. Introducing avelumab after a patient achieves stable disease with first-line platinum-containing chemotherapy, is an alternative treatment approach that offers the potential to delay progression resulting in extended overall survival and delays later line treatment options. This treatment regimen of maintenance with avelumab after induction with platinum-containing chemotherapy significantly improves overall survival fulfilling the unmet need for a novel treatment approach early in the treatment pathway that improves patient outcomes regardless of their PD-L1 status.	Comment noted. No action required.
	Fight Bladder Cancer	Very urgent. At the moment there is no approved maintenance therapy after first-line chemotherapy of advanced bladder cancer.	Comment noted. NICE schedules technology

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			appraisals so that guidance to the NHS is timely. For cancer drugs, NICE aims to publish final guidance within 90 days of marketing authorisation wherever possible.

Comment 2: the draft scope

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Background information	Merck Serono Ltd	Background information is considered accurate apart from information on pembrolizumab for treatment after platinum-containing chemotherapy which as part of the CDF review was not recommended for baseline commissioning [ID1536] (https://www.nice.org.uk/guidance/gid-ta10466/documents/final-appraisal-determination-document)	Comment noted. ID1536 has yet to published as final guidance and therefore TA519 remains the current guidance at this time.
	Fight Bladder Cancer	The statement "In 2017, 8,686 new bladder cancers were diagnosed in England" only includes advanced cases (C67). We suggest stating instead "In 2017, 17,921 new bladder cancers were diagnosed in England". Reference: https://www.cancerdata.nhs.uk/getdataout/bladder Furthermore, this sentence should be added: "68% of bladder cancer deaths in the UK are in males, and 32% are in females". Reference:	Comment noted. The updated background information clarifies “In 2017, 8,686 new *invasive* bladder cancers were diagnosed in England.”

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		https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer/mortality#heading-Zero	
The technology/ intervention	Merck Serono Ltd	Description of the technology is accurate. For completeness, additional information on avelumab has been provided below: Avelumab has been shown to induce natural killer cell-mediated direct tumour cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro. Avelumab is administered by intravenous infusion at a flat dose of 800mg. Avelumab currently has marketing authorisation in the UK for a number of indications, including: • as monotherapy for the treatment of adult patients with metastatic Markel cell carcinoma (MCC) • in combination with axitinib for the first-line treatment of adult patients with advanced renal cell carcinoma (aRCC).	Comment noted. This section is intended to give a brief overview of the technology. No action required.
	Fight Bladder Cancer	Yes.	Comment noted. No action required.
Population	Merck Serono Ltd	The population is defined appropriately. In line with the specification of the Population to be assessed as described in the draft scope *"Adults with locally advanced or metastatic urothelial cancer whose disease did not progress while on or after completion of first-line platinum-based chemotherapy",* it is the company's interpretation that any analysis comparing avelumab as a first-line maintenance therapy to treatment strategies which do not first include platinum-based chemotherapy would not be relevant to the current technology appraisal. Therefore, no analyses are	Comment noted. No action required.

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		planned for submission as part of this technology appraisal which assess a population of mUC patients prior to completion (without progression) of a first-line platinum-based chemotherapy regimen	
	Fight Bladder Cancer	Yes	Comment noted. No action required.
Comparators	Merck Serono Ltd	1. Yes, patients that complete 1st line treatment are often put on a wait and watch strategy before commencing 2nd line treatment, with supportive care provided to alleviate specific symptoms. 2. Yes, this can be described as 'best alternative care'	Comment noted. No action required.
	Fight Bladder Cancer	Yes.	Comment noted. No action required.
Outcomes	Merck Serono Ltd	These outcome measures sufficiently capture the most important health related benefits (and harms) of the technology.	Comment noted. No action required.
	Fight Bladder Cancer	Yes.	Comment noted. No action required.
Economic analysis	Fight Bladder Cancer	The time horizon should be at least 24-36 months, to reflect any differences in costs or outcomes between the technologies	Comment noted. No action required.
Innovation	Merck Serono Ltd	Avelumab as first-line maintenance therapy is innovative in its potential to make a significant and substantial impact on health-related benefits and can be considered a step-change in management when considering its clinical trial results:	Comment noted. The appraisal committee will consider any innovative aspects of avelumab as part of its decision

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		• Avelumab is the first immunotherapy to demonstrate in a Phase III clinical trial a statistically significant improvement in OS as a first-line treatment for patients with locally advanced or metastatic UC • Avelumab is the first treatment to be appraised as a first-line maintenance treatment following induction with platinum-containing chemotherapy, with the aim of improving the durability of the response to the induction therapy and to improve the long-term disease outcomes All health-related benefits of avelumab will likely be captured in the QALY calculation in the cost-effectiveness analysis.	making. No action required.
	Fight Bladder Cancer	Yes, this technology could be a step change for the treatment in this setting. It will be important to review Quality of Life data between this technology and supportive care.	Comment noted. The appraisal committee will consider any innovative aspects of avelumab as part of its decision making. No action required.