NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of avelumab within its marketing authorisation for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy.

Background

Urothelial carcinoma is cancer of the transitional cells which form the inner lining of the bladder, urethra, ureter, or renal pelvis. Urothelial carcinoma is most common in the bladder, and accounts for approximately 90% of bladder cancers.[1] Urothelial carcinomas can be described as non-invasive or invasive depending on how far the carcinomas invade the tissues. Non-invasive urothelial carcinomas can be further split into papillary carcinomas or flat carcinomas. Papillary carcinomas often grow towards the hollow part of the organ (for example bladder and ureter), without going into deeper layers. Flat carcinomas remain in the inner layers. Both papillary and flat carcinomas can become invasive.

In 2017, 8,686 new bladder cancers were diagnosed in England[2]. Bladder cancer accounts for around 1 in every 30 new cancer diagnoses each year in the UK, and is the 10th most common cancer in the UK[3]. The majority of new cases are in those over the age of 75 but can also affect young people too. 72% of bladder cancer cases in the UK are in males, and 28% are in females[4]. Smoking is a major factor in the cause of bladder cancer.

People with muscle invasive urothelial cancer may have surgery and/or radiotherapy. Chemotherapy may be given before (neoadjuvant) surgery and/or radiotherapy in an attempt to improve cure rates. If the cancer is too advanced for surgery/radiotherapy or has recurred after these treatments, chemotherapy can be used to improve quality of life and survival. NICE guideline NG2 recommends cisplatin-based regimens (such as gemcitabine plus cisplatin or accelerated [high dose] methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]) for untreated disease. Carboplatin plus gemcitabine may be considered for untreated disease if cisplatin is unsuitable.

There are no maintenance treatments currently licensed for use after response to first-line platinum-containing chemotherapy. However for people with locally advanced or metastatic urothelial carcinoma whose disease has progressed after platinum-containing chemotherapy, atezolizumab is recommended in NICE technology appraisal 525 and pembrolizumab is recommended within the Cancer Drugs Fund (at the time the draft scope was written) in NICE technology appraisal 519.

The technology

Avelumab (Bavencio, Merck Serono Ltd) is an anti-PD-L1 monoclonal antibody with a dual mechanism of action. It aims to bind and block the inhibitory signalling through PD-1/PD-L1 resulting in the activation of T-cells and cell-mediated immune responses against tumour cells or pathogens. Avelumab is administered by intravenous infusion.

Avelumab does not currently have a marketing authorisation in the UK for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy. It has been studied in a clinical trial in adults with locally advanced or metastatic urothelial cancer whose disease did not progress after completion of first-line platinum-containing chemotherapy. Avelumab in combination with best supportive care was compared with best supportive care only.

Intervention(s)	Avelumab
Population(s)	Adults with locally advanced or metastatic urothelial cancer whose disease did not progress while on or after completion of first-line platinum-based chemotherapy.
Comparators	Established clinical management without avelumab (including but not limited to routine surveillance, symptom control, and pain management [including palliative radiotherapy])
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to relapse or progression • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 525. Review date: June 2021. Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (2018). NICE Technology Appraisal 530. Review date: July 2021. Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 519. Pembrolizumab subject to ongoing NICE CDF review (ID1536), expected date of publication to be confirmed. Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract (2013). NICE Technology Appraisal 272. Transferred to the static list November 2015. **Appraisals in development (including suspended appraisals):** Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. NICE technology appraisals guidance [ID1333]. Publication date to be confirmed. Durvalumab for treating metastatic urothelial bladder cancer after chemotherapy. Suspended NICE technology appraisals guidance [ID1172]. Durvalumab for untreated PD-L1 positive metastatic urothelial bladder cancer. NICE technology appraisals guidance [ID1169]. Publication date to be confirmed. Durvalumab with tremelimumab for untreated PD-L1-positive urothelial bladder cancer. NICE technology appraisals guidance [ID1335]. Publication date to be confirmed. **Related Guidelines:** Bladder cancer: diagnosis and management (2015) NICE guideline NG2. Improving outcomes in urological cancers (2002) NICE cancer service guidance. Published September 2002. **Related Interventional Procedures:** Laparoscopic cystectomy NICE interventional procedure

	guidance 287. Published February 2009. Electrically-stimulated intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 277. Published November 2008 Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 235. Published October 2007. **Related Quality Standards:** Bladder cancer NICE quality standard. Published December 2015. **Related NICE Pathways:** Bladder cancer (2019) NICE Pathway.
Related National Policy	NHS England (2019) Specialised kidney, bladder and prostate cancer services (adults) The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for avelumab been included in the scope?

How should 'established clinical management without avelumab' be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom avelumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider avelumab will fit into the existing NICE pathway, 'Bladder cancer'?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which avelumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider avelumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of avelumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Cancer Research UK (2018) Types of bladder cancer. Accessed April 2020.

2. Office for National Statistics (2019) Cancer Registration Statistics, England: 2017. Accessed April 2020.

3. Cancer Research UK (2018) Bladder cancer statistics. Accessed April 2020.

4. Cancer Research UK (2018) Bladder cancer incidence statistics. Accessed April 2020.