**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

# Atezolizumab for untreated PD-L1 positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (CDF review TA492)

**Final scope**

## Remit

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for treating locally advanced or metastatic urothelial carcinoma in people whose disease has progressed after prior chemotherapy or for whom cisplatin-based chemotherapy is unsuitable.[1]

## Appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for treating locally advanced or metastatic urothelial carcinoma in people who are considered cisplatin ineligible and whose tumours have a PD-L1 expression of 5% or more.

## Background

Urothelial carcinoma is cancer of the transitional cells which form the inner lining of the bladder, urethra, ureter, or renal pelvis. Transitional cell cancer (TCC) of the renal pelvis and ureter is rare and in the UK accounts for only about 7 out of 100 kidney cancers, and is 4 times less common in the ureter. Urothelial carcinoma is most common in the bladder, and accounts for 90% of bladder cancers[1].

Transitional cell cancers can be split into papillary carcinomas and flat carcinomas. Papillary carcinomas often grow towards the centre of the bladder, without going into deeper layers (non-invasive) but sometimes these can grow deeper into the bladder wall and are more likely to spread (invasive). Flat carcinomas do not grow toward the hollow part of the bladder and remain in the inner layers (non-invasive). Other types of bladder cancers include squamous cell carcinoma (beginning in thin flat cells) and adenocarcinoma (beginning in cells which make and release mucus and other fluids). These types of bladder cancer arise as a result of chronic irritation and inflammation.

There were 10,300 diagnoses of bladder cancer in 2013, accounting for 1 in every 30 new cases of cancer each year[2, 3]. Overall incidence is 11.4 per

[1] The remit that was issued in 2016 is broader than the scope of this review. There is separate guidance on atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy

100,000 and is more common in men than women (3:1)[2]. The majority of cases are in those over the age of 60 but can also affect young people too[3, 4]. Smoking is major factor in the cause of bladder cancer[4].

Patients with metastatic or advanced urothelial cancer may receive treatment with surgery and/or radiotherapy. Chemotherapy may be given before (neoadjuvant) or after surgery and/or radiotherapy in an attempt to improve cure rates. If the urothelial 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 methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]) for untreated disease or after one prior therapy. In addition, carboplatin plus gemcitabine maybe considered for untreated disease. In people for whom cisplatin is unsuitable, and their tumours express PD-L1 at a level of 5% or more, NICE technology appraisal 492 recommends atezolizumab within the Cancer Drugs Fund.

## The technology

Atezolizumab (Tecentriq, Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Atezolizumab has a marketing authorisation in UK for treating adult patients with locally advanced or metastatic urothelial carcinoma (UC) after prior platinum-containing chemotherapy, or who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression ≥ 5%.

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| **Intervention(s)** | Atezolizumab |
| **Population(s)** | Adults with untreated PD-L1 positive locally advanced or metastatic urothelial cancer, for whom cisplatin based chemotherapy is unsuitable and whose tumours have a PD-L1 expression ≥ 5 |

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| **Comparators** | • Gemcitabine plus carboplatin<br>• Best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• adverse effects of treatment<br>• 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.<br>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 .<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention or comparator technologies will be taken into account. |

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| **Other considerations** | The economic modelling should include the costs associated with any diagnostic testing in people with urothelial cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals<br><br>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:**<br>Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. (2013) NICE technology appraisal guidance 272. Reviewed November 2015. Decision to transfer to static list.<br><br>Atezolizumab for untreated locally advanced or metastatic urothelial carcinoma when cisplatin is unsuitable. NICE technology appraisal guidance 492. Review date December 2020.<br><br>Pembrolizumab for locally advanced or metastatic urothelial cancer where cisplatin is unsuitable. NICE technology appraisal guidance 674 (2021). (Terminated Appraisal).<br><br>**Appraisals in development (including suspended appraisals):**<br><br>Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy. NICE technology appraisal guidance [ID3735]. Expected date of publication June 2021.<br><br>Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. NICE technology appraisals guidance [ID1333]. Publication date to be confirmed.<br><br>Durvalumab for untreated PD-L1 positive metastatic urothelial bladder cancer. NICE technology appraisals guidance [ID1169]. Publication date to be confirmed.<br><br>Durvalumab with tremelimumab for untreated PD-L1-positive urothelial bladder cancer. NICE technology appraisals guidance [ID1335]. Publication date to be confirmed. |

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| | Pembrolizumab with chemotherapy for untreated metastatic urothelial cancer. NICE technology appraisal guidance [ID1545]. Publication date to be confirmed.<br><br>**Related Guidelines:**<br>Bladder cancer: diagnosis and management (2015) NICE guideline NG2. Reviewed 2019 (no new evidence was found that affects the recommendations in this guideline).<br><br>Improving outcomes in urological cancers (2002) NICE cancer service guidance. Published September 2002.<br><br>**Related Interventional Procedures:**<br><br>Laparoscopic cystectomy NICE interventional procedure guidance 287. Published February 2009.<br><br>Electrically-stimulated intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 277. Published November 2008.<br><br>Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 235. Published October 2007.<br><br>**Related Quality Standards:**<br>Bladder cancer NICE quality standard. Published December 2015.<br><br>**Related NICE Pathways:**<br>Bladder cancer (2019) |
| **Related National Policy** | NHS England (2019) Specialised kidney, bladder and prostate cancer services (adults)<br><br>The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)<br><br>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 |

## References


1. Transitional cell cancer, Cancer Research UK. Accessed September 2016.

2. Bladder Cancer statistics, Cancer Research UK. Accessed July 2016.

3. Bladder Cancer, Patient UK. Accessed July 2016.

4. The facts about Bladder cancer, Action Bladder Cancer UK. Accessed July 2016.