NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Atezolizumab with gemcitabine and carboplatin for untreated metastatic urothelial bladder cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab with gemcitabine and carboplatin within its marketing authorisation for treating untreated metastatic urothelial bladder cancer.

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 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 2016, 8,500 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, with an overall incidence of around 17 per 100,000.[3] About a quarter of bladder cancers are diagnosed at a late stage[4].The majority of cases are in those over the age of 60 but can also affect young people too.

People with locally advanced or metastatic urothelial cancer may have 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 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. 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. Where cisplatin is unsuitable and tumours express PD-L1 with a combined positive score of 10 or more, NICE

technology appraisal 522 recommends pembrolizumab within the Cancer Drugs Fund[a].

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 with gemcitabine and carboplatin does not currently have a marketing authorisation in the UK for untreated urothelial cancer. It has been studied in a clinical trial compared to chemotherapy alone in people with untreated advanced urothelial cancer.

Intervention(s)	Atezolizumab with gemcitabine and carboplatin
Population(s)	People with locally advanced or metastatic urothelial carcinoma.
Comparators	People for whom cisplatin-based chemotherapy is suitable: • Gemcitabine plus cisplatin • Accelerated methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) plus granulocyte-colony stimulating factor (G-CSF) People for whom cisplatin-based chemotherapy is unsuitable: • Gemcitabine plus carboplatin • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

[a] Products recommended for use in the Cancer Drugs Fund after 1 April 2016 should not be considered as comparators, or appropriately included in a treatment sequence, in subsequent relevant appraisals. https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisal-guidance/cancer-drugs-fund/CDF-comparator-position-statement.pdf

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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 patient access schemes for the intervention or comparator technologies will be taken into account. The use of atezolizumab with gemcitabine and carboplatin is conditional on the presence of PD-L1. The economic modelling should include the costs associated with diagnostic testing for PD-L1 in people with locally advanced or metastatic urothelial carcinoma 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.
Other considerations	If the evidence allows, consideration will be given to subgroups based on the biological marker PD-L1. 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:** Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (2018) NICE technology appraisal guidance 530 Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018) NICE technology appraisal guidance 525 Pembrolizumab for locally advanced or metastatic urothelial cancer where cisplatin is unsuitable. NICE technology appraisal guidance 522 Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy

	(2018) NICE technology appraisal guidance 519 Atezolizumab for untreated locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (2017) NICE technology appraisal guidance 492 **Appraisals in development:** Durvalumab for untreated PD-L1 positive metastatic urothelial bladder cancer. NICE technology appraisal guidance [ID1169]. Publication date to be confirmed. Durvalumab with tremelimumab for untreated PD-L1-positive urothelial bladder cancer. NICE technology appraisal guidance [ID1335]. Publication date to be confirmed. Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy. NICE technology appraisal guidance [ID1536]. Publication date to be confirmed. **Related Guidelines:** Bladder cancer: diagnosis and management (2015) NICE guideline 2. Review date 2019. Improving outcomes in urological cancers (2002) NICE cancer service guidance. Review date March 2020. **Related Interventional Procedures:** Laparoscopic cystectomy (2009) NICE interventional procedures guidance 287 Electrically-stimulated intravesical chemotherapy for superficial bladder cancer (2008). NICE interventional procedure guidance 277. Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer (2007). NICE interventional procedure guidance 235. **Related Quality Standards:** Bladder cancer (2015) NICE quality standard. **Related NICE Pathways:** Bladder cancer (2018) NICE Pathway.
Related National Policy	Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy The NHS Long Term Plan, 2019. NHS Long Term Plan

	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105 specialist cancer services (adults) Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017

Questions for consultation

Have all relevant comparators for atezolizumab with gemcitabine and carboplatin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic urothelial cancer?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom atezolizumab with gemcitabine and carboplatin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider atezolizumab with gemcitabine and carboplatin will fit into the existing NICE pathway on 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 atezolizumab with gemcitabine and carboplatin 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 atezolizumab with gemcitabine and carboplatin 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 atezolizumab with gemcitabine and carboplatin 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK (2015) Types of bladder cancer. Accessed October 2019.
2. Office for National Statistics (2018) Cancer Registration Statistics, England: 2016. Accessed October 2019.
3. Cancer Research UK (2016) Bladder cancer incidence statistics. Accessed October 2019.
4. Cancer Research UK (2016) Bladder cancer incidence statistics. Accessed October 2019.

