

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

### Pembrolizumab for advanced, unresectable or metastatic urothelial cancer (CDF review TA522) [ID1634]

#### Final scope

#### Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating locally advanced or metastatic urothelial carcinoma in people for whom cisplatin-based chemotherapy is unsuitable.

#### Background

Urothelial carcinoma is cancer of the transitional cells that 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.<sup>1</sup> 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 2015, 8,500 new bladder cancers were diagnosed in England.<sup>2</sup> 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.<sup>3</sup> The majority of cases are in those over the age of 60 but can also affect young people too, and is more common in men than women (around 3:1).<sup>3</sup> Smoking is a major factor in the cause of bladder cancer.

People with locally advanced or metastatic urothelial carcinoma 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 cancer is too advanced for surgery/radiotherapy or has recurred after these treatments, first-line chemotherapy can be used to improve quality of life and survival. NICE guideline NG2 recommends carboplatin plus gemcitabine for people with locally advanced or metastatic urothelial bladder cancer for whom cisplatin-based chemotherapy regimen is unsuitable. Best supportive care may also be offered to people with locally advanced or metastatic urothelial bladder cancer.

#### The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune

suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

When the final scope for technology appraisal guidance 522 was issued by NICE in September 2017, the Committee for Medicinal Products for Human Use (CHMP) had recommended that a marketing authorisation be granted for pembrolizumab for treating locally advanced or metastatic urothelial carcinoma in people for whom cisplatin-based chemotherapy is unsuitable. In July 2018 the European Medicines Agency restricted the use of pembrolizumab for untreated urothelial carcinoma. Pembrolizumab has a marketing authorisation for ‘the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more’.

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| <b>Intervention(s)</b> | Pembrolizumab  |
| <b>Population(s)</b>   | Adults with locally advanced or metastatic urothelial carcinoma for whom cisplatin-based chemotherapy is unsuitable  |
| <b>Comparators</b>     | <ul style="list-style-type: none"> <li>• Carboplatin plus gemcitabine</li> <li>• <del>Atezolizumab (subject to ongoing NICE appraisal)<sup>1</sup></del></li> <li>• Best supportive care</li> </ul>  |
| <b>Outcomes</b>        | <p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul> |

<sup>1</sup> NICE recommended atezolizumab for use within the Cancer Drugs Fund as an option for untreated locally advanced or metastatic urothelial carcinoma in adults when cisplatin-containing chemotherapy is unsuitable (TA492). 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>

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| <p><b>Economic analysis</b></p>                              | <p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>  |
| <p><b>Other considerations</b></p>                           | <p>If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1).</p> <p>If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices.</p> <p>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.</p>   |
| <p><b>Related NICE recommendations and NICE Pathways</b></p> | <p>Related Technology Appraisals:</p> <p><a href="#">‘Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract’</a> (2013) NICE technology appraisal 272. Static list: January 2016.</p> <p><a href="#">‘Pembrolizumab for previously treated advanced or metastatic urothelial cancer’</a> (2018) NICE technology appraisal guidance 519.</p> <p><a href="#">‘Atezolizumab for treating locally advanced or metastatic urothelial carcinoma’</a> (2018) NICE technology appraisal 492.</p> <p>Related Guidelines:</p> <p><a href="#">‘Bladder cancer: diagnosis and management’</a> (2015) NICE guideline NG2. Review date: 2019.</p> <p><a href="#">‘Improving outcomes in urological cancers’</a> (2002) NICE guideline CSG2. Review date: March 2020.</p> |

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|                                       | <p>Related Quality Standards:</p> <p><a href="#">‘Bladder cancer’</a> (2015) NICE quality standard 106.</p> <p>Related NICE Pathways:</p> <p><a href="#">‘Bladder cancer’</a> (2016) NICE pathway.</p>   |
| <p><b>Related National Policy</b></p> | <p>Department of Health <a href="#">Cancer research and treatment</a></p> <p>Department of Health (2016) <a href="#">NHS outcomes framework 2016 to 2017</a>: Domain 1.</p> <p>Department of Health (2014) <a href="#">The national cancer strategy: 4<sup>th</sup> annual report</a></p> <p>NHS England (2016) <a href="#">Manual for Prescribed Specialised Services 2016/17</a>. Chapter 105. Specialist cancer services (adults).</p> <p>NHS England (2013) <a href="#">B14. Cancer: Specialised kidney, bladder and prostate cancer services (Adult). NHS Standard Contract.</a></p> <p>NHS England (2013) <a href="#">B15. Cancer: Chemotherapy (Adult). NHS Standard Contract.</a></p> <p>Independent Cancer Taskforce (2015) <a href="#">Achieving world-class cancer outcomes: a strategy for England 2015-2020</a></p> |

## References

1. Cancer Research UK (2015) [Types of bladder cancer](#). Accessed September 2017.
2. Office for National Statistics (2017) [Cancer Registration Statistics, England: 2015](#). Accessed September 2017.
3. Cancer Research UK (2016) [Bladder cancer incidence statistics](#). Accessed September 2017.