

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

**Enfortumab vedotin with pembrolizumab for first-line treatment of unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy [ID6332]**

**Final scope**

**Remit/evaluation objective**

To appraise the clinical and cost effectiveness of enfortumab vedotin with pembrolizumab within its marketing authorisation for treating adult patients with untreated unresectable or metastatic urothelial cancer who are eligible for platinum-containing 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 accounts for approximately 90% of bladder cancers.<sup>1</sup> Urothelial cancer can also originate in the upper urinary tract. 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 2020, 16,547 new bladder cancers were diagnosed in England.<sup>2</sup> Bladder cancer is the 11th most common cancer in the UK.<sup>3,4</sup> The majority of cases are in those over the age of 75 but can also affect young people too and is more common in men than women with incidences of 22.8 and 8.3 per 100,000 respectively.<sup>3,4</sup> Smoking is a major factor in the cause of bladder cancer.

People with urothelial carcinoma may receive treatment with surgery and/or radiotherapy. Treatment 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, treatments can be used to improve quality of life and survival.

The first-line treatment options for locally advanced or metastatic urothelial carcinoma in adults include a cisplatin-based chemotherapy regimens, or carboplatin in combination with gemcitabine if a cisplatin-based chemotherapy regimen is unsuitable. Methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] in combination with granulocyte-colony stimulating factor [G-CSF] may also be used. Atezolizumab is also an option if a cisplatin-based chemotherapy regimen is unsuitable and tumours express PD-L1 at a level of 5% or more.

**The technology**

Pembrolizumab (Keytruda, MSD) with enfortumab vedotin (Padcev, Astellas) does not currently have a marketing authorisation in the UK for treating untreated metastatic urothelial cancer. The combination has been studied in clinical trials compared with chemotherapy alone in adults with untreated locally advanced or untreated metastatic urothelial cancer.

Pembrolizumab has a marketing authorisation for locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy, and for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express programmed death-ligand 1 with a combined positive score  $\geq 10$ .

Enfortumab vedotin has a marketing authorisation for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and a programmed death receptor-1 or programmed death-ligand 1 inhibitor.

<b>Intervention(s)</b>	Enfortumab vedotin in combination with pembrolizumab
<b>Population(s)</b>	People with untreated unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy
<b>Subgroups</b>	<p>If the evidence allows the following subgroups will be considered:</p> <ul style="list-style-type: none"> <li>• People for whom cisplatin containing chemotherapy is unsuitable</li> <li>• People whose tumours express PD-L1</li> </ul>
<b>Comparators</b>	<p>For people whom cisplatin-based chemotherapy is suitable:</p> <ul style="list-style-type: none"> <li>• Gemcitabine plus cisplatin</li> <li>• Methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]</li> </ul> <p>For people whom cisplatin-based chemotherapy is unsuitable:</p> <ul style="list-style-type: none"> <li>• Gemcitabine plus carboplatin</li> <li>• Atezolizumab (people whose tumours express PD-L1 at a level of 5% or more)</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>

<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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<p><b>Other considerations</b></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</b></p>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable</a> (2017). NICE Technology Appraisal 739. Review date: 2024.</p> <p><a href="#">Pembrolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable</a> (2018). NICE Technology Appraisal 674. Terminated appraisal.</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. Transferred to the static list November 2015.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Suspected cancer: recognition and referral</a> (2023) NICE guideline NG12.</p> <p><a href="#">Bladder cancer: diagnosis and management</a> (2015) NICE guideline NG2.</p> <p><a href="#">Improving outcomes in urological cancers</a> (2002) NICE cancer service guidance.</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Bladder cancer</a> NICE quality standard. Published December 2015.</p> <p><b>Related NICE Pathways:</b></p>

	<a href="#">Bladder cancer</a> (2019) NICE Pathway
<b>Related National Policy</b>	<p>NHS England (2019) <a href="#">Specialised kidney, bladder and prostate cancer services (adults)</a></p> <p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

**References**

1. Cancer Research UK (2023) [Types of bladder cancer](#). Accessed October 2023
2. National Disease Registration Service (2023) [Bladder cancer statistics Get Data Out programme](#). Accessed March 2024
3. NHS Digital (2022) [Cancer Registration Statistics, England 2020](#). Accessed October 2023
4. Patient (2021) [Bladder Cancer -Diagnosis, Symptoms, and Treatment](#). Accessed October 2023