

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with enfortumab vedotin for untreated metastatic urothelial cancer

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with enfortumab vedotin within its marketing authorisation for treating untreated locally advanced or metastatic urothelial 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 accounts for approximately 90% of bladder cancers.¹ 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, 8,752 new bladder cancers were diagnosed in England.² Bladder cancer is the 11th most common cancer in the UK.³ 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.^{2,3} 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 or atezolizumab if a cisplatin-based chemotherapy regimen is unsuitable.

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 unresectable 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 ≥ 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.

Intervention(s)	Pembrolizumab in combination with enfortumab vedotin
Population(s)	People with untreated locally advanced or metastatic urothelial cancer
Comparators	<p>For people whom cisplatin-based chemotherapy is suitable:</p> <ul style="list-style-type: none"> • Gemcitabine plus cisplatin • Methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF] • Best supportive care <p>For people whom cisplatin-based chemotherapy is unsuitable:</p> <ul style="list-style-type: none"> • Gemcitabine plus carboplatin • Atezolizumab • Best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</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>Other considerations</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>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (2017). NICE Technology Appraisal 492. Review date: December 2020.</p> <p>Pembrolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (2018). NICE Technology Appraisal 522. Review date to be confirmed.</p> <p>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.</p> <p>Related Guidelines:</p> <p>Suspected cancer: recognition and referral (2023) NICE guideline NG12.</p> <p>Bladder cancer: diagnosis and management (2015) NICE guideline NG2.</p> <p>Improving outcomes in urological cancers (2002) NICE cancer service guidance.</p> <p>Related Quality Standards:</p> <p>Bladder cancer NICE quality standard. Published December 2015.</p>

	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

Where do you consider pembrolizumab with enfortumab vedotin will fit into the existing care pathway for urothelial cancer?

Have all relevant comparators for pembrolizumab with enfortumab vedotin been included in the scope?

If the evidence allows, should subgroups by PD-L1 expression be considered?

Would pembrolizumab with enfortumab vedotin be a candidate for managed access?

Do you consider that the use of pembrolizumab with enfortumab vedotin can result in any potential 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 committee to take account of these benefits.

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 pembrolizumab with enfortumab vedotin 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. Cancer Research UK (2023) [Types of bladder cancer](#). Accessed October 2023
2. NHS Digital (2022) [Cancer Registration Statistics, England 2020](#). Accessed October 2023
3. Patient (2021) [Bladder Cancer -Diagnosis, Symptoms, and Treatment](#). Accessed October 2023