

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Enfortumab vedotin for treating locally advanced or metastatic urothelial cancer after platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of enfortumab vedotin within its marketing authorisation for treating locally advanced or metastatic urothelial cancer after platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor.

Background

Urothelial carcinoma is cancer of the transitional cells which make up the inner lining of the bladder, urethra, ureter, or renal pelvis. It is most common in the bladder, and accounts for around 90% of bladder cancers.¹ Bladder cancer is the ninth most common cancer overall in the UK and the sixth most common in men.² There are over 20,000 new bladder cancer cases in the UK each year³ (of which over 9,000 are muscle-invasive⁴), and it is more common in people aged 75 and over.⁴ Smoking, multiple bladder infections, long-lasting bladder irritation and chemical exposure are some of the risk factors in developing bladder cancer.^{2,5,6}

Approximately 18,000 people are diagnosed with bladder cancer each year in England³ (of which around 8,000 have muscle-invasive cancer⁷), and around a quarter of people have locally advanced or metastatic disease at the time of their initial diagnosis.² Even with recent advances in treatment (such as immunotherapy) after several decades of platinum-based therapy being standard of care, prognosis is poor for people with metastatic urothelial cancer (median survival of 15 to 18 months).²

Typically, people with locally advanced or metastatic urothelial cancer initially have platinum, such as a cisplatin-based chemotherapy regimen, or carboplatin with gemcitabine. Where cisplatin is unsuitable, atezolizumab (NICE technology appraisal [TA]492) is available via the Cancer Drugs Fund, depending on the level of PD-L1 expression. If the disease progresses, NICE guideline 2 recommends chemotherapy regimens, such as paclitaxel with gemcitabine or carboplatin, gemcitabine with cisplatin or accelerated (high-dose) MVAC (methotrexate, vinblastine, doxorubicin and cisplatin) in combination with granulocyte-colony stimulating factor. Atezolizumab (TA525) is recommended for people who have had platinum-containing chemotherapy. Nivolumab (TA530) and vinflunine (TA272) are not recommended for bladder cancer. Pembrolizumab after platinum-containing chemotherapy is not recommended (TA692).

For people whose disease has progressed and have no further options, then NICE guideline 2 suggests treatment aimed at aimed at relief of symptoms. This may include palliative chemotherapy or palliative radiotherapy.

The technology

Enfortumab vedotin (Padcev, Astellas Pharma) is a monoclonal anti-nectin-4 antibody coupled with a microtubule disrupting agent, and is given intravenously.

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Issue Date: April 2021

Appendix B

Enfortumab vedotin does not currently have a marketing authorisation in the UK for urothelial cancer. It has been studied in a clinical trial compared to chemotherapy (docetaxel, paclitaxel or vinflunine), in adults whose locally advanced or metastatic cancer has progressed or relapsed after treatment with an immune checkpoint inhibitor (targeting the PD-L1 or PD-1 pathway) and platinum-based chemotherapy.

Intervention(s)	Enfortumab vedotin
Population(s)	People with locally advanced or metastatic urothelial cancer who have had a platinum-containing chemotherapy and a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor
Comparators	<ul style="list-style-type: none"> • Chemotherapy (may include docetaxel or paclitaxel) • 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
Economic analysis	<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 and comparator(s) will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.</p>
Other considerations	<p>The availability and cost of biosimilar and generic products should be taken into account.</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>If evidence allows, the following sub-groups should be considered: levels of nectin-4 expression.</p>

<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy. NICE technology appraisal [TA692]. Review date to be confirmed.</p> <p>Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy. NICE technology appraisal [TA530]. Review date 2021.</p> <p>Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. NICE technology appraisal [TA272]. Reviewed January 2016.</p> <p>Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable. NICE technology appraisal [TA492]. Review date October 2021.</p> <p>Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy. NICE technology appraisal [TA525]. Review date 2021.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (CDF Review of TA492) [ID3777]. Expected publication October 2021.</p> <p>Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy. NICE technology appraisal [ID3735]. Expected publication June 2021.</p> <p>Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. Proposed NICE technology appraisal [ID1333]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>Bladder cancer: diagnosis and management (2015). NICE guideline 2. Reviewed April 2019.</p> <p>Improving supportive and palliative care for adults with cancer (2004). NICE cancer service guideline 4</p> <p>Improving outcomes in urological cancers (2002). NICE cancer service guideline 2</p> <p>Related Public Health Guidance:</p> <p>Guidance for management of urothelial cancer during COVID-19 (2020) Royal College of Radiologists</p> <p>Related Quality Standards:</p> <p>Bladder cancer (2015) NICE quality standard 106</p> <p>Related NICE Pathways:</p>
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	Bladder cancer (2019) NICE pathway https://pathways.nice.org.uk/pathways/bladder-cancer
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapters 105 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

- 1 Cancer Research UK (2018) Types of bladder cancer. Accessed January 2021.
- 2 Cheeseman S, Thompson M, Sopwith W et al. (2020) Current treatment and outcomes benchmark for locally advanced or metastatic urothelial cancer from a large UK-based single centre. *Frontiers in Oncology* 10.
- 3 Fight Bladder Cancer (year unknown) My diagnosis counts. Accessed April 2021.
- 4 Cancer Research UK (year unknown). Bladder cancer statistics. Accessed January 2021.
- 5 Di Lorenzo G, Buonerba C, Bellelli T et al. (2015) Third-line chemotherapy for metastatic urothelial cancer: a retrospective observational study. *Medicine (Baltimore)* 94(51):e2297.
- 6 Cancer Research UK (2019) Bladder cancer: risks and causes. Accessed January 2021.
- 7 Office for National Statistics (2019). Cancer registration statistics, England: 2017. Accessed January 2021.