Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Enfortumab vedotin for treating locally advanced or metastatic urothelial cancer after 2 therapies

Draft scope

Draft 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 2 therapies.

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 around 10,000 new bladder cancer cases in the UK each year, and 56% of these diagnoses in people aged 75 and over.[3] Smoking, multiple bladder infections, long-lasting bladder irritation and chemical exposure are some of the risk factors in developing bladder cancer.[2,4,5]

Approximately 8,700 people are diagnosed with bladder cancer each year in England,[6] and around a quarter 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) and pembrolizumab (TA522) are available via the Cancer Drugs Fund, depending on the level of PD-L1 expression. NICE guideline 2 recommends chemotherapy regimens for second line treatment, 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. Another recommended second therapy option is atezolizumab (TA525). Taxanes such as docetaxel or paclitaxel might be used in clinical practice. Pembrolizumab (TA519, review ongoing) is available in second line only via the Cancer Drugs Fund. Nivolumab (TA530) and vinflunine (TA272) are not recommended for bladder cancer.

There are currently no routinely recommended drug treatments in the NHS for people with locally advanced or metastatic urothelial cancer, who have experienced progression or relapse of their cancer after first and second line treatments. Currently, treatment after second line is aimed at relief of symptoms. NICE guideline 2 suggests approaches for people who have had 2 therapies, according to their symptoms and overall fitness. This includes chemotherapy, best supportive care or palliative care (which may include chemotherapy or 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.

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 programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and who have had a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting
Comparators	• Chemotherapy (may include docetaxel or paclitaxel) • Best supportive care • Palliative care (which may include chemotherapy or radiotherapy)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life
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. 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 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.

Other considerations	The availability and cost of biosimilar and generic products should be taken into account. 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: Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy. NICE technology appraisal [TA519]. Being reviewed as ID1536, expected publication April 2021. Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy. NICE technology appraisal [TA530]. Review date 2021. Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. NICE technology appraisal [TA272]. Reviewed January 2016. Pembrolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable. NICE technology appraisal [TA522]. Review date TBC. Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable. NICE technology appraisal [TA492]. Review date TBC. Appraisals in development (including suspended appraisals) Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy. NICE technology appraisal [ID1536]. Expected publication April 2021. Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy. NICE technology appraisal [ID3735]. Expected publication June 2021. Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. Proposed NICE technology appraisal [ID1333]. Publication date to be confirmed. Related Guidelines: Bladder cancer: diagnosis and management (2015). NICE guideline 2. Reviewed April 2019. Improving supportive and palliative care for adults with cancer (2004). NICE cancer service guideline 4 Improving outcomes in urological cancers (2002). NICE cancer service guideline 2

	Related Public Health Guidance: Guidance for management of urothelial cancer during COVID-19 (2020) Royal College of Radiologists Related Quality Standards: Bladder cancer (2015) NICE quality standard 106 Related NICE Pathways: 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

Questions for consultation

Does the population defined in the scope reflect the treatments that people with locally advanced or metastatic urothelial cancer have in the NHS?

Have all relevant comparators for enfortumab vedotin been included in the scope? Are any listed which aren't used in NHS practice for this point in the pathway? Which treatments are considered to be established clinical practice in the NHS for urothelial cancer after 2 therapies? What chemotherapy regimens would be given at this point in the treatment pathway?

How should best supportive care be defined? How should palliative care be defined in this particular setting? What differentiates chemotherapy, best supportive care and palliative care in this stage of the treatment pathway?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom enfortumab vedotin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider enfortumab vedotin will fit into the existing NICE pathway, 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 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.

Do you consider enfortumab vedotin 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 enfortumab vedotin 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).

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 Cancer Research UK (year unknown). Bladder cancer statistics. Accessed January 2021.

4 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.

5 Cancer Research UK (2019) Bladder cancer: risks and causes. Accessed January 2021.

6 Office for National Statistics (2019). Cancer registration statistics, England: 2017. Accessed January 2021.

