NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with enfortumab vedotin for neoadjuvant and adjuvant treatment of muscle-invasive bladder cancer [ID6607]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with enfortumab vedotin within its marketing authorisation for neoadjuvant and adjuvant treatment of muscle-invasive bladder cancer.

Background

Bladder cancer is where a growth of abnormal tissue, known as a tumour, develops in the bladder lining. Muscle-invasive bladder cancer is when cancerous cells spread beyond the lining into the surrounding bladder muscle. Common symptoms of bladder cancer include blood in the urine, passing urine often, pain or burning sensation when passing urine, fatigue, pain in lower back or abdomen and unexplained weight loss.

In 2023, 18,389 new bladder cancer cases were diagnosed in England.[1] At diagnosis, 30% of bladder cancers are muscle-invasive bladder cancer.[2] Most cases are in people over 75 but bladder cancer can affect young people too.[3] Bladder cancer is more common in men than in women,[3] although women are more likely to be diagnosed at a later stage.[4] Smoking is a significant risk factor for bladder cancer.[5]

NICE guideline NG2 recommends people with muscle-invasive bladder cancer may have surgery or radiotherapy. This is offered with curative intent. Cisplatin combination chemotherapy is recommended before surgery (neoadjuvant), although many people with muscle-invasive bladder cancer cannot have cisplatin-based therapy. This may be, for example, because of frailty or comordibities. Surgery consists of radical cystectomy (removal of the bladder) with urinary stoma or a continent urinary diversion. After surgery, some people with high risk of recurrence (for example positive lymph-node involvement) or for whom neoadjuvant chemotherapy was not suitable may receive cisplatin-based adjuvant therapy to improve survival. Where adjuvant platinum-based chemotherapy is not suitable, NICE technology appraisal 817 recommends nivolumab as an option for the adjuvant treatment of muscle-invasive urothelial cancer that is at high risk of recurrence after radical resection in adults whose tumours express programmed death-ligand 1 inhibitor (PD-L1) at a level of 1% or more.

The technology

Pembrolizumab (Keytruda, MSD) with enfortumab vedotin (Padcev, Astellas) does not currently have a marketing authorisation in the UK for neoadjuvant and adjuvant treatment of muscle-invasive bladder cancer. The combination has been studied in clinical trials with pembrolizumab for perioperative treatment of muscle-invasive bladder cancer, both in people who can have and cannot have or decline cisplatin.

Pembrolizumab with enfortumab vedotin does have a marketing authorisation in the UK for the first-line treatment of unresectable or metastatic urothelial cancer in adults. Pembrolizumab also has a marketing authorisation in the UK for treating locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy, and in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express PD-L1 with a combined positive score ≥ 10. Enfortumab vedotin also has a marketing authorisation in the UK for the treatment of locally advanced or metastatic urothelial cancer in adults who have previously received a platinum-containing chemotherapy and a programmed death receptor-1 (PD-1) or PD-L1.

Intervention	Pembrolizumab with enfortumab vedotin
Population	People with muscle-invasive bladder cancer who are having radical cystectomy
Subgroups	If the evidence allows, the following subgroups will be considered: • People who can have cisplatin-based therapy • People who cannot have cisplatin-based therapy • Results by level of PD-L1 expression
Comparators	For neoadjuvant treatment: • Cisplatin-based chemotherapy • No active treatment • Durvalumab with gemcitabine and cisplatin For adjuvant treatment: • Cisplatin-based chemotherapy • Nivolumab (for muscle-invasive urothelial cancer that is at high risk of recurrence after radical resection in adults whose tumours express PD-L1 at a level of 1% or more, and when platinum-based chemotherapy is unsuitable) • No active treatment • Durvalumab

Outcomes	The outcome measures to be considered include: • event-free survival • disease-free survival • overall 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, comparator and subsequent treatment technologies will be taken into account. The availability and biosimilar and generic products should be taken into account.
Other considerations	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	**Related technology appraisals:** Nivolumab for adjuvant treatment of invasive urothelial cancer at high risk of recurrence. (2022) NICE technology appraisal guidance 817 **Related technology appraisals in development:** Durvalumab with gemcitabine and cisplatin before surgery (neoadjuvant) then alone after surgery (adjuvant) for treating muscle-invasive bladder cancer. NICE technology appraisal guidance [ID6168] Publication date to be confirmed. Nivolumab with BMS-986205 and chemotherapy for neoadjuvant treatment of muscle-invasive bladder cancer. NICE technology appraisal guidance [ID6321] Publication date to be confirmed **Related NICE guidelines:**

	Bladder cancer: diagnosis and management (2015) NICE guideline NG2. Suspected cancer: recognition and referral (2023) NICE guideline NG12 **Related quality standards:** Bladder cancer (2015) NICE quality standard 106.

References

1. Cancer registration statistics (2023). Cancer registration statistics in England (Accessed November 2025)

2. Saginala, K. et al (2020) Epidemiology of bladder cancer, Med. Sci 8(1): 15

3. Cancer Research UK Bladder cancer incidence statistics. (Accessed November 2025)

4. Action Bladder Cancer The Facts About Bladder Cancer (Accessed February 2026)

5. Cancer Research UK Bladder cancer risk (Accessed November 2025)