

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pembrolizumab for previously treated advanced or metastatic urothelial cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating locally advanced and unresectable or metastatic urothelial cancer in adults whose disease has progressed on or after prior platinum-containing chemotherapy.

Background

Urothelial carcinoma is cancer of the transitional cells (TCC) which form the inner lining of the bladder, urethra, ureter, or renal pelvis. Urothelial carcinoma is most common in the bladder and accounts for 90% of urothelial cancers. Most urothelial cell carcinomas of the bladder are TCCs, which can be split into papillary carcinomas and flat carcinomas. Papillary carcinomas often grow towards the centre of the bladder, without going into deeper layers (non-invasive) but sometimes these can grow deeper into the bladder wall and are more likely to spread (invasive). Flat carcinomas do not grow toward the hollow part of the bladder and remain in the inner layers (non-invasive). Other types of bladder cancers include squamous cell carcinoma (beginning in thin flat cells) and adenocarcinoma (beginning in cells which make and release mucus and other fluids). These types of bladder cancer arise as a result of chronic irritation and inflammation.

There were 10,300 diagnoses of bladder cancer in 2013, accounting for 1 in every 30 new cases of cancer each year^{1, 2}. Overall incidence is 11.4 per 100,000 and is more common in men than women (3:1)². The majority of cases are in those over the age of 60 but can also affect younger people too^{2, 3}. Smoking is a major factor in the cause of bladder cancer³.

Patients with metastatic or advanced urothelial cancer may receive treatment with surgery and/or radiotherapy. Chemotherapy may be given before (neoadjuvant) or after surgery and/or radiotherapy in an attempt to improve cure rates. If the urothelial cancer is too advanced for surgery/radiotherapy or has recurred after these treatments, chemotherapy can be used to improve quality of life and survival. NICE guideline NG2 recommends cisplatin-based regimens (such as gemcitabine plus cisplatin or accelerated methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]) for untreated disease or after one prior therapy. In addition, carboplatin plus gemcitabine maybe considered for untreated disease and carboplatin or gemcitabine plus paclitaxel may be considered after one prior

therapy. For people whose disease has progressed after platinum-based chemotherapy, a taxane such as docetaxel or paclitaxel may be given. Vinflunine is not recommended for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract that has progressed after treatment with platinum-based chemotherapy ([NICE technology appraisal 272](#)).

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK for treating locally advanced or metastatic urothelial bladder cancer after prior platinum-based chemotherapy. It is being studied in a phase III clinical trial as monotherapy in adults with locally advanced and unresectable or metastatic urothelial cancer that has progressed following a platinum-containing regimen, compared with vinflunine, paclitaxel, or docetaxel.

Intervention	Pembrolizumab
Population	Adults with locally advanced and unresectable or metastatic urothelial cancer that has progressed on or after platinum-containing chemotherapy.
Comparators	<ul style="list-style-type: none"> • Retreatment with 1st line platinum-based chemotherapy (only for people whose disease has had an adequate response) • Docetaxel • 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 (e.g. duration of response and disease control rate) • 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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<p>Other considerations</p>	<p>If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-1 or CD274 antigen).</p> <p>If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices.</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 and NICE Pathways</p>	<p>Related Technology Appraisals: Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. (2013) NICE technology appraisal guidance 272. Reviewed November 2015. Decision to transfer to static list.</p> <p>Atezolizumab for treating metastatic urothelial bladder after platinum-based chemotherapy NICE technology appraisal ID939. Expected publication date: September 2017</p> <p>Related Guidelines: Bladder cancer: diagnosis and management (2015) NICE guideline NG2.</p> <p>Improving outcomes in urological cancers (2002) NICE cancer service guidance. Published September 2002.</p> <p>Related Interventional Procedures: Laparoscopic cystectomy NICE interventional procedure guidance 287. Published February 2009.</p>

	<p>Electrically-stimulated intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 277. Published November 2008</p> <p>Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 235. Published October 2007.</p> <p>Related Quality Standards: Bladder cancer NICE quality standard. Published December 2015</p> <p>Related NICE Pathways: Bladder cancer (2015) NICE pathway.</p>
Related National Policy	<p>National Service Frameworks Cancer</p> <p>Other policies Department of Health (2016) NHS outcomes framework 2016 to 2017</p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>Department of Health (2011) Improving outcomes: a strategy for cancer</p> <p>Department of Health (2009) Cancer commissioning guidance</p> <p>Department of Health (2007) Cancer reform strategy</p>

References

1. Bladder Cancer statistics, [Cancer Research UK](#). Accessed July 2016
2. Bladder Cancer, [Patient UK](#). Accessed July 2016
3. The facts about Bladder cancer, [Action Bladder Cancer UK](#). Accessed July 2016