

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with lenvatinib within its marketing authorisation for treating previously treated advanced, metastatic or recurrent endometrial cancer.

Background

Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. It is the most common type of womb cancer and often diagnosed in the earlier stages. When diagnosed, endometrial cancer is categorised between stage 1 and 4. Advanced endometrial cancer is defined as stage 3 or 4, where the cancer has spread outside the womb. In stage 3 the spread of cancer is contained within the pelvis, once the cancer has spread into another area of the body it is classed as stage 4 or metastatic (stages 3 and 4 are known as advanced cancer). Recurrent endometrial cancer is when the cancer returns after primary treatment. The cancer can recur anywhere, common areas include the abdominal cavity, lymph nodes, lung and vagina. The symptoms of recurrence are variable but include abdominal pain, bloating, nausea, shortness of breath, vaginal bleeding and changes in bowel or bladder habits¹.

There are approximately 9,400 new cases of endometrial cancer every year in the UK. Around 2,400 deaths occurred in 2018 which accounts for 3% of all cancer deaths in females in the UK. Only 15% of women diagnosed with advanced or recurrent endometrial cancer at late stage survive for more than 5 years, compared to 92% of women diagnosed at early stage². Less than 5% of endometrial cancers occur in women under 45 years of age³.

The first treatment for endometrial cancer is usually removal of the womb (hysterectomy) as well as both fallopian tubes and ovaries (bilateral salpingo-oophorectomy). In advanced endometrial cancer, debulking surgery may be carried out to remove as much of the cancer as possible⁴. Radiotherapy may be used for people who cannot have surgery, or alongside surgical treatment. Platinum-based chemotherapy can be used as an adjunct to surgery for people with stage 2 to 4 disease. Hormone therapy with progestins, or platinum-based chemotherapy may be used for cancer that has metastasised or relapsed.

The technologies

Pembrolizumab (Keytruda, MSD) 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.

Lenvatinib (Lenvima, Eisai) is a multiple receptor tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor (VEGF) receptors and other

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receptor tyrosine kinases that are involved in tumour proliferation. It is administered orally.

Pembrolizumab with lenvatinib has a marketing authorisation in the UK for treatment of advanced or recurrent endometrial cancer in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.

Intervention(s)	Pembrolizumab with lenvatinib
Population(s)	People with advanced, metastatic or recurrent endometrial cancer, previously treated with platinum-based therapy who are not able to receive curative surgery or radiation.
Comparators	<ul style="list-style-type: none"> • Chemotherapy, including: <ul style="list-style-type: none"> - Carboplatin and paclitaxel - Paclitaxel monotherapy - Doxorubicin monotherapy - Carboplatin monotherapy • Hormone therapy (such as medroxyprogesterone acetate and megestrol) • Best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression-free survival • overall survival • response rates • duration of response • 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, comparator and subsequent treatment technologies will be taken into account.</p>

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 and NICE Pathways	<p>Appraisals in development:</p> <p>Dostarlimab for previously treated recurrent or advanced endometrial cancer with high microsatellite instability or mismatch repair deficiency [ID3802]. Publication expected January 2022</p> <p>Pembrolizumab for previously treated endometrial cancer. Proposed NICE technology appraisal [ID1205]. Suspended appraisal.</p> <p>Related NICE Pathways:</p> <p>Urogenital conditions (2020) NICE pathway http://pathways.nice.org.uk/pathways/urogenital-conditions</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

References

- 1 Murali R, Soslow RA, Weigelt B (2014) Classification of endometrial carcinoma: more than two types. *The Lancet. Oncology* 15(7): 268-278.
- 2 Cancer Research UK (2017) Uterine cancer statistics. Accessed September 2020.
- 3 British Gynaecological Cancer Society (2017) BGCS uterine cancer guidelines: recommendations for practice. Accessed September 2020.
- 4 NHS (2018) Treatment: Womb (uterus) cancer. Accessed September 2020.