NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenvatinib with pembrolizumab for previously treated advanced, metastatic or recurrent endometrial cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenvatinib with pembrolizumab 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 are 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 habits[1].

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. An estimated figure of 71.6% of women diagnosed with uterine cancer in England survive for ten years or more[2]. Less than 5% of endometrial cancers occur in women under 45 years of age[3].

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 possible[4]. Radiotherapy may be used for people who cannot have surgery, or alongside surgical treatment. Platinum based chemotherapy can be used adjunct to surgery for people with stage 2-4 disease. Hormone therapy with progestins, or platinum-based chemotherapy may be used for cancer that has metastasised or relapsed.

The technologies

Lenvatinib (Kisplyx, Eisai) is a multiple receptor tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor (VEGF) receptors and other receptor tyrosine kinases that are involved in tumour proliferation. It is administered orally.

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 with pembrolizumab does not currently have a marketing authorisation in the UK for previously treated advanced endometrial cancer. The combined therapy is being studied in clinical trials for patients with previously treated advanced, endometrial cancer whose disease has progressed after platinum-based chemotherapy regimen.

Intervention(s)	Lenvatinib with pembrolizumab
Population(s)	People with previously treated advanced, metastatic or recurrent endometrial cancer
Comparators	• Chemotherapy (such as paclitaxel, carboplatin, cisplatin, doxorubicin and cyclophosphamide) • Hormone therapy (such as medroxyprogesterone acetate and megestrol) • Best supportive care
Outcomes	The outcome measures to be considered include: • progression-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.
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	Proposed Technology Appraisals: Pembrolizumab for previously treated endometrial cancer. Proposed NICE technology appraisal [ID1205]. Publication date to be confirmed. Dostarlimab for previously treated recurrent or advanced endometrial cancer with high microsatellite instability or mismatch repair deficiency [ID3802]. Publication date to be confirmed. Related NICE Pathways: Urogenital conditions (2020) NICE pathway http://pathways.nice.org.uk/pathways/urogenital-conditions
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan 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

Questions for consultation

Is the population in the scope defined appropriately?

Have all relevant comparators for lenvatinib with pembrolizumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for previously treated advanced, metastatic and recurrent endometrial cancer? How should best supportive care be defined?

Are the outcomes listed appropriate?

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

Where do you consider lenvatinib with pembrolizumab will fit into the existing NICE pathway for endometrial cancer, Urogenital conditions?

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 lenvatinib with pembrolizumab 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 lenvatinib with pembrolizumab 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 lenvatinib with pembrolizumab 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 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.