NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Olaparib for maintenance treatment of BRCA 1 or 2 mutated, relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people whose relapsed disease has responded to platinum-based chemotherapy

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of olaparib within its licensed indication for maintenance treatment of BRCA 1 or 2 mutated relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people whose relapsed disease has responded to platinum-based chemotherapy.

Background

Ovarian cancer represents a group of tumours that arise from diverse types of tissue contained in the ovary. The most common type of ovarian cancer arises from epithelial cells on the surface of the ovary, and can often spread from the ovary to any surface within the abdominal cavity including the fallopian tubes and peritoneal cavity. Fallopian tube cancer and primary peritoneal cancer are histologically equivalent diseases to epithelial ovarian cancer. Ovarian cancer is classified from stage I to stage IV. Advanced ovarian cancer falls within stages III and IV; stage III denotes disease that is locally advanced and has spread outside the pelvis into the abdominal cavity and stage IV denotes that distant metastasis to other body organs such as the liver and lungs has occurred. Most people are diagnosed with advanced stage disease. Some people have gene mutations that may increase the risk of ovarian cancer. Mutated inherited genes that increase the risk of ovarian cancer include BRCA 1 or 2.

The incidence of ovarian cancer increases with age, with 75% of diagnoses in people over 55 years. Approximately 10% of ovarian cancers occur in people with mutations in genes BRCA 1 or 2. In 2011, approximately 5900 people were diagnosed with ovarian cancer in England and in 2012 there were 3500 deaths from ovarian cancer in England. The overall 5-year survival rate for ovarian cancer is approximately 43%.

Ovarian cancer may be categorised according to the response to initial platinum chemotherapy as follows: platinum-sensitive (disease responds to platinum-based therapy but relapses after 6 months or more, which can be subdivided into fully [disease responds to platinum-based therapy but relapses after 12 months or more] and partially platinum-sensitive disease [disease responds to platinum-based therapy but relapses between 6 and 12 months]); platinum-resistant (disease which relapses within 6 months of

completion of platinum-based chemotherapy) and platinum-refractory, that is, does not respond to initial platinum-based chemotherapy. Although a significant percentage of people have disease that responds to initial chemotherapy, between 55% and 75% of people whose tumours respond to initial therapy relapse within 2 years of completing treatment.

In people whose disease relapses following initial therapy, NICE technology appraisal guidance 91 (currently under review) recommends paclitaxel in combination with a platinum compound in platinum-sensitive or partially platinum-sensitive disease; pegylated liposomal doxorubicin hydrochloride in partially platinum-sensitive, platinum-resistant or platinum-refractory disease; paclitaxel alone in platinum-refractory or platinum-resistant disease; and topotecan in platinum-refractory or platinum-resistant disease for people for whom pegylated liposomal doxorubicin hydrochloride and single-agent paclitaxel are considered inappropriate. There are currently no treatments licensed for the maintenance treatment of relapsed, platinum-sensitive ovarian cancer.

The technology

Olaparib (Lynparza; AstraZeneca) is a poly-ADP-ribose polymerase (PARP) enzyme inhibitor which selectively kills tumour cells with an impaired homologous recombination DNA repair pathway whilst sparing normal cells. It is administered orally.

Olaparib monotherapy has received CHMP positive opinion for the maintenance treatment of platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer in adults whose disease is in response (complete response or partial response) to platinum-based chemotherapy.

Intervention(s)	Olaparib
Population(s)	People with BRCA 1 or 2 mutated, relapsed, platinum-sensitive ovarian, fallopian tube or peritoneal cancer whose relapsed disease has responded to platinum-based chemotherapy.
Comparators	Routine surveillance

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • progression-free survival 2 (i.e. progression-free survival on next line of therapy) • time to next line of therapy • 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.
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 in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. The use of olaparib is conditional on the presence of BRCA 1 or 2 mutation. The economic modelling should include the cost associated with the diagnostic testing for BRCA 1 or 2 mutations in people with ovarian cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 55, Jan 2003. 'Review of the clinical effectiveness and cost effectiveness of paclitaxel for ovarian cancer'. Transferred to the static guidance list. Technology Appraisal No. 91, May 2005, 'Topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for the treatment of advanced ovarian cancer'.

	Currently under review in combination with TA 222. Technology Appraisal No. 222, Apr 2011, 'Trabectedin for the treatment of relapsed ovarian cancer'. Currently under review in combination with TA 91. Technology Appraisal No. 285, May 2013. 'Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer'. Review proposal date June 2016. Technology Appraisal in Preparation, 'Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for advanced ovarian cancer (for recurrent disease only) (Review of TA 91 and TA 222)' Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline No. 122, April 2011, 'The recognition and initial management of ovarian cancer'. Review Proposal Date April 2014. Clinical Guideline No. 164, June 2013, 'Familial breast cancer'. Review Proposal Date TBC. Related Interventional Procedures: Interventional Procedure No. 470, November 2013, 'Ultra-radical (extensive) surgery for advanced ovarian cancer'. Related Quality Standards: Quality Standard No. 18, May 2012, 'Ovarian cancer' Review Proposal Date May 2017 http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Ovarian cancer, Pathway created: February 2012 http://pathways.nice.org.uk/pathways/ovarian-cancer http://pathways.nice.org.uk/
Related National Policy	Department of Health, December 2013, 'Improving outcomes: a strategy for cancer third annual report'