NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Olaparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people who have tested positive for BRCA 1 or 2 mutations, following response to prior platinum-based chemotherapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of olaparib within its licensed indication for the maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people who have tested positive for BRCA 1 or 2 mutations, following response to prior platinum-based chemotherapy.

Background

Ovarian cancer represents a group of different tumours that arise from diverse types of tissue contained in the ovary. The most common type of ovarian cancer arises from epithelial cells (the outside layer of 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 women 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 over 80% of diagnoses in women over 50 years. Approximately 10% of ovarian cancers occur in women with mutations in genes BRCA 1 or 2. In 2010, approximately 5800 women were diagnosed with ovarian cancer in England and in 2008 there were approximately 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); 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

women have disease that responds to initial chemotherapy, between 55% and 75% of women 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 (brand name unknown; 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 does not currently have a UK marketing authorisation for the maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people who have tested positive for BRCA 1 or 2 mutations, following response to prior platinum-based chemotherapy. It has been studied in clinical trials compared with placebo in adults with relapsed, platinum-sensitive high grade serous ovarian cancer (including primary peritoneal and fallopian tube cancer) and high grade endometrial cancer who have tested positive for BRCA 1 or 2 mutations and whose disease has responded to platinum-based chemotherapy.

Intervention(s)	Olaparib
Population(s)	People with relapsed, platinum-sensitive ovarian, fallopian tube or peritoneal cancer who have tested positive for BRCA 1 or 2 mutations and whose disease has responded to platinum therapy.
Comparators	Established clinical practice without olaparib (including routine surveillance)

Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 55, January 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 February 2014. Technology Appraisal in Preparation, 'Pazopanib for maintenance treatment of epithelial ovarian, fallopian and peritoneal cancer'. Earliest anticipated date of publication April 2015. Related Guidelines: Clinical Guideline No. 122, April 2011, 'The recognition and initial management of ovarian cancer'. Review Proposal Date April 2014. Related Interventional Procedures: Interventional Procedure in Preparation, 'Ultra-radical (extensive) surgery for advanced ovarian cancer' Earliest anticipated date of publication Autumn 2013 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	'Improving Outcomes: A Strategy for Cancer, second annual report, 2012', March 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/136551/Improving_outcomes_second_annual_report.pdf

Questions for consultation

Have all relevant comparators for olaparib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for the maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer in people who have tested positive for BRCA 1 or 2 mutations, following response to prior platinum-based chemotherapy?

Is bevacizumab an appropriate comparator for olaparib?

Are there any subgroups of people in whom olaparib is expected to be more clinically effective and cost effective or other groups that should be examined separately, for example subgroups based on response to platinum-based chemotherapy (complete or partial response)?

Where do you consider olaparib will fit into the existing NICE pathway, Ovarian cancer?

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 olaparib 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 the technology 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 the technology 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.

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)