NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Rucaparib for treating relapsed ovarian, fallopian tube or peritoneal cancer that has a BRCA mutation

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rucaparib within its marketing authorisation for treating relapsed, BRCA mutated ovarian, fallopian tube or peritoneal cancer.

Background

Ovarian cancer is a cancerous growth that occurs in different parts of the ovary or fallopian tubes. The most common type of ovarian cancer, high-grade serous type, is thought to arise from the peritoneum or fallopian tube and presents after it has spread to the ovary. Ovarian cancer is classified from stage I to stage IV. Advanced ovarian cancer falls within stages II and IV; in stage II the disease has grown outside the ovaries but is still within the pelvic area, 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 the pleura (two thin layers of tissue that protect and cushion the lungs) has occurred. Most people are diagnosed with advanced stage disease.

BRCA 1 or 2 mutations can be inherited mutations present in all cells (germline) or non-inherited mutations that occur in ovarian tissue (somatic). Germline mutations increase the risk of developing ovarian cancer. It is estimated that 15% of people diagnosed with ovarian cancer have a germline BRCA 1 or 2 mutation, and that 9% have a somatic mutation[1].

The incidence of ovarian cancer increases with age and average age at diagnosis is 63 years[2]. In 2015, 6,198 people were diagnosed with ovarian cancer in England and there were 3,352 deaths from ovarian cancer[3]. The 5-year survival for people diagnosed with ovarian cancer between 2010 and 2014 and followed up to 2015, in England was 49.5%[4].

Ovarian cancer may be categorised according to the response to 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.

NICE technology appraisal guidance 389 recommends paclitaxel as monotherapy or in combination with platinum, and pegylated liposomal doxorubicin hydrochloride as monotherapy or in combination with platinum, for treating recurrent ovarian cancer. In addition, NICE technology appraisal 381 recommends olaparib as an option for maintenance treatment of relapsed, platinum sensitive ovarian, fallopian tube or peritoneal cancer in adults who have BRCA 1 or 2 mutations and whose disease has responded to platinum based chemotherapy, if they have had 3 or more courses of platinum based chemotherapy.

The technology

Rucaparib (Rubraca, Clovis Oncology) is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes including PARP-1, PARP-2 and PARP-3, which play a role in DNA repair. Rucaparib is administered orally.

Rucaparib does not currently have a marketing authorisation in the UK for treating ovarian cancer. It has been studied in single arm trials in patients with relapsed, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who received prior platinum-based regimens. It is also being compared with chemotherapy in people with relapsed or progressive epithelial ovarian, fallopian tube, or primary peritoneal cancer who have a BRCA 1 or 2 mutation and who have received at least 2 prior lines of therapy.

Intervention(s)	Rucaparib monotherapy
Population(s)	People with BRCA mutated (germline or somatic) ovarian, fallopian tube or peritoneal cancer who have received 2 or more prior courses of chemotherapy
Comparators	• Paclitaxel with or without platinum based chemotherapy • Pegylated liposomal doxorubicin hydrochloride[1] with or without platinum based chemotherapy • Gemcitabine in combination with carboplatin For people with platinum sensitive disease only: • Platinum based chemotherapy followed by maintenance treatment with olaparib in those who respond to chemotherapy

[1] Use in combination with platinum based chemotherapy is outside the marketing authorisation for pegylated liposomal doxorubicin hydrochloride.

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 patient access schemes for the intervention or comparator technologies will be taken into account. 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, for example testing for somatic mutations. 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.
Other considerations	Where evidence is available, consideration will be given to subgroups with platinum-sensitive and platinum-resistant disease. 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	Related Technology Appraisals: Olaparib for maintenance treatment of relapsed, platinum-sensitive, BRCA mutation-positive ovarian, fallopian tube and peritoneal cancer after response to second-line or subsequent platinum-based chemotherapy (2016) NICE technology appraisal guidance 381. Review date 2 years after publication or when trial results are available. Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer (2016) NICE technology appraisal guidance 389. Review date April 2019. Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer (2013) NICE technology appraisal guidance 285. Reviewed May 2013, guidance on static list. Appraisals in development (including suspended appraisals) Ovarian cancer – niraparib [ID1041]. Expected date of publication: March 2018. Ovarian (epithelial), fallopian and peritoneal cancer - pazopanib (maintenance) [ID545]. Suspended. Ovarian cancer - vintafolide (with pegylated liposomal doxorubicin) [ID564]. Suspended. Related Guidelines: Ovarian cancer: recognition and initial management (2011) NICE guideline CG122. Review date to be confirmed Related Quality Standards: Ovarian cancer (2012) NICE quality standard 18 Related NICE Pathways: Ovarian cancer (2016) NICE Pathway

Related National Policy	NHS England (April 2014) Complex Gynaecology - Specialist Gynaecological Cancers. Clinical Commissioning Policy. Reference E10/S/f NHS England (October 2015) Clinical Commissioning Policy: Genetic Testing for BRCA1 and BRCA2 Mutations. Clinical Commissioning Policy. Reference E01/P/b NHS England (April 2015) Complex Gynaecology – Severe Endometriosis. Clinical Commissioning Policy. Reference E01/S/a https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Angela George (2015), UK BRCA mutation testing in patients with ovarian cancer, British Journal of Cancer

2. Patient (2013). Ovarian Cancer 2013. Accessed November 2016.

3. Office for National Statistics (2015) Death Registrations Summary Tables – England and Wales. Accessed June 2017.

4. Office for National Statistics (2014). Cancer survival in England: Patients diagnosed between 2010 and 2014 and followed up to 2015. Accessed January 2017.