NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Rucaparib for maintenance treatment of recurrent platinum-sensitive epithelial ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of rucaparib within its marketing authorisation for maintenance treatment of recurrent platinum-sensitive epithelial ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy.

Background

Ovarian cancer is a cancerous growth that occurs in 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. 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 and 2.

The incidence of ovarian cancer increases with age and average age at diagnosis is 65 years[1]. In 2016, 6,430 people were diagnosed with ovarian cancer in England and there were 3,693 deaths from ovarian cancer in 2016[2,3]. The 5-year survival for women diagnosed with ovarian cancer between 2011 and 2015 and followed up to 2016, in England was 42.9%[4].

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 recurs after 12 months or more] and partially platinum-sensitive disease [disease responds to platinum-based therapy but recurs between 6 and 12 months]); platinum-resistant (disease which recurs 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 who relapse following initial therapy, 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. 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 BRCA1 or BRCA2 mutations and whose disease has responded to platinum based chemotherapy, if they have had 3 or more courses of platinum based chemotherapy (this guidance is currently under review). In addition, NICE technology appraisal 528 recommends niraparib for use within the Cancer Drugs Fund as an option for maintenance treatment of relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to the most recent course of platinum-based chemotherapy: in people who have a germline BRCA mutation and have had 2 courses of platinum-based chemotherapy and people who do not have a germline BRCA mutation and have had 2 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 maintenance treatment of ovarian cancer. It has been studied in a clinical trial, compared with placebo, as maintenance treatment in patients with platinum-sensitive relapsed, high-grade epithelial ovarian, fallopian tube, and/or primary peritoneal cancer. People in the trial had received at least 2 previous courses of platinum-containing therapy and their disease had responded (completely or partially) to the most recent chemotherapy containing a platinum agent.

Rucaparib has a marketing authorisation for the following related indication: ‘treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy’.

Intervention(s)	Rucaparib
Population(s)	People with recurrent platinum-sensitive epithelial ovarian, fallopian tube or peritoneal cancer that is in response (complete or partial) to platinum-based chemotherapy
Comparators	• Routine surveillance For people who have BRCA1 or BRCA2 mutations and who have responded to the third or subsequent course of platinum based chemotherapy: • Olaparib (subject to ongoing appraisal)
Outcome	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. 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 diagnostic testing in people with platinum-sensitive ovarian, fallopian tube and peritoneal 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'.

Other considerations	If the evidence allows, consideration will be given to subgroups with or without BRCA mutations. 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:** Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer (2018) NICE technology appraisal guidance TA528. Review date July 2020 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 381 Currently under review 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 285. Reviewed in June 2016, guidance on static list **Appraisals in development:** Olaparib for maintenance treatment of recurrent, platinum-sensitive ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy (including a review of technology appraisal no. 381) NICE technology appraisal guidance [ID1296]. Publication expected January 2019 **Suspended technology appraisals:** Ovarian, fallopian tube and peritoneal cancer – rucaparib. NICE technology appraisal guidance

	[ID1184]. Suspended September 2017. Ovarian cancer (platinum sensitive) - cediranib [ID790]. NICE technology appraisal guidance. Suspended September 2016. Ovarian (epithelial), fallopian and peritoneal cancer - pazopanib (maintenance) [ID545]. NICE technology appraisal guidance. Suspended April 2014. Ovarian cancer - vintafolide (with pegylated liposomal doxorubicin) [ID564]. NICE technology appraisal guidance. Suspended July 2014. **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** NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a. NHS England. 2013/14 NHS Standard Contract for Cancer: Gynaecological. E10/S/f/. **Other policies** Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Public Health England (2015) Living with and beyond ovarian cancer Department of Health (2014) The national cancer strategy: 4th annual report

References

1. Patient (2013). Ovarian Cancer 2013. Accessed August 2018.

2. Office for National Statistics (2016). Cancer Registration Statistics, England 2016. Accessed August 2018

3. Office for National Statistics (2016) Death Registrations Summary Tables – England and Wales. Accessed August 2018.

4. Office for National Statistics (2014). Cancer survival in England: Patients diagnosed between 2010 and 2014 and followed up to 2015. Accessed August 2018.