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Health Technology Briefing
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Olaparib maintenance therapy for non-gBRCA mutated high-grade serous ovarian cancer after platinum-based chemotherapy

Company/Developer	AstraZeneca UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 24099	NICE ID: 10749	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Olaparib is in clinical development for the maintenance treatment of adults with platinum-sensitive non-germline breast cancer susceptibility gene (non-gBRCA) mutated high-grade serous ovarian cancer, including fallopian tube cancer or primary peritoneal cancer. These cancers occur in the female reproductive system and are often grouped together as they are treated in the same way. Tumours can occur in the ovaries, fallopian tubes or peritoneum. Non-gBRCA disease occurs when the growth of the tumour is not driven by an inherited abnormality in a gene known as BRCA. High-grade serous disease is a type of cancer characterised by its appearance when viewed under a microscope. Platinum-sensitive disease occurs when a patient has previously responded to treatment with chemotherapy including a platinum-based drug, but relapses after 6 months or more. There are currently no maintenance therapies for ovarian, fallopian tube and peritoneal cancer which are recommended specifically for the treatment of non-gBRCA disease.

Olaparib is a drug given as an oral tablet or capsule, which blocks the ability of human proteins to repair damaged DNA and therefore can limit the growth of tumours. Olaparib is currently recommended as a maintenance treatment for ovarian, fallopian tube and peritoneal cancer. Olaparib has demonstrated positive treatment outcomes in clinical trials targeting non-gBRCA ovarian, fallopian tube and peritoneal cancer. If licensed, olaparib would provide a targeted treatment option for this patient group.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Proposed Indication

Maintenance treatment of female adults with platinum-sensitive relapsed non-germline breast cancer susceptibility gene (non-gBRCA) mutated high-grade serous ovarian cancer, including primary peritoneal and/or fallopian tube cancer, who are in complete or partial response following platinum-based chemotherapy.[1]

Technology

Description

Olaparib (Lynparza) is an inhibitor of human poly (ADP-ribose) polymerase enzymes (PARP-1, PARP-2 and PARP-3). PARPs are required for the efficient repair of DNA single strand breaks and an important aspect of PARP-induced repair requires that after chromatin modification, PARP auto-modifies itself and dissociates from the DNA to facilitate access for base excision repair (BER) enzymes. When olaparib is bound to the active site of DNA-associated PARP, it prevents the dissociation of PARP and traps it on the DNA, thus blocking repair. Olaparib has been shown to inhibit the growth of selected tumour cell lines.[2]

Olaparib is currently in phase III clinical development for the maintenance treatment of female adults with platinum-sensitive relapsed non-gBRCA mutated ovarian cancer who are in complete or partial response following platinum-based chemotherapy. In the phase III clinical trial (OPINION, NCT03402841), patients were administered olaparib 300mg twice daily via oral tablet until disease progression or unacceptable toxicity.[1,3]

Key Innovation

Olaparib is currently licensed as a maintenance therapy for ovarian cancer patients who have advanced germline and/or somatic BRCA mutations.[2] In the SOLO2 clinical trial (NCT00753545), olaparib showed significant clinical benefit also for non-gBRCA mutated patients.[4] Studies show that olaparib given on its own increases the time women with cancer of the ovary, fallopian tube or peritoneum live without their disease getting worse in those patients whom treatment with platinum-based chemotherapy has shrunk or cleared the cancer.[5]

Regulatory & Development Status

Olaparib has a Marketing Authorisation in the UK for the following indications:[2]

- As a monotherapy for the maintenance treatment of adults with advanced (FIGO stages III and IV) BRCA/12-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy
- As a monotherapy for the maintenance treatment of adults with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy
- In combination with bevacizumab for the maintenance treatment of adults with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in combination with bevacizumab and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either a BRCA1/2 mutation and/or genomic instability
- As a monotherapy for the treatment of adults with germline BRCA1/2-mutations who have HER2 negative locally advanced or metstatic breast cancer. Patients should have been previously treated with an anthracycline and a taxane in the neoadjuvant or metastatic setting unless it was not suitable

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- As a monotherapy for the maintenance treatment of adults with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen
- As a monotherapy for the treatment of adults with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent

Olaparib as a monotherapy or in combination with various other medicinal products is being developed for several indications in phase II and phase III clinical trials, some of which include:[6]

- Endometrial cancer
- Breast cancer
- Prostate cancer
- Colorectal cancer
- Pancreatic cancer

Patient Group

Disease Area and Clinical Need

Epithelial ovarian cancer, fallopian tube cancer and primary peritoneal cancers are cancerous growths that occur in the female reproductive system. All three cancers form from the same tissues and are all treated in the same way. They can occur in the ovaries, the fallopian tubes or the peritoneum.[7] High-grade serous cancers are the most common type of ovarian cancer and are thought to arise from the peritoneum or fallopian tube and spread to the ovaries, where it presents with symptoms. Platinum-sensitive disease refers to disease which has responded to platinum-based chemotherapy but has subsequently relapsed after 6 months or more.[8] Histologically, high-grade serous tumours refer to tumour cells characterised by cells with solid mass and slit-like fenestrations.[9] Non-gBRCA mutated patients do not have inherited mutations in the BRCA 1 and 2 genes that produce proteins to help repair damaged DNA.[10] Potential risk factors for developing ovarian cancer can include older age, genetic mutations, previous cancers, hormone replacement therapy (HRT) use and smoking.[11]

In 2016-18, there were an average of 7,495 cases of ovarian cancer each year in the UK.[12] In England in 2020-21, there were 29,984 hospital admissions for malignant neoplasm of ovary (ICD10 C56) and 2,305 hospital admissions for malignant neoplasm: fallopian tube (ICD10 C57).[13] In 2017, the age-standardised incidence rate was 20.6 per 100,000 for new diagnoses of malignant neoplasm of the ovary.[14] Approximately 43% of patients diagnosed with ovarian cancer will survive for five years following diagnosis.[15]

Recommended Treatment Options

NICE do not currently recommend any maintenance treatments targeted at patients with non-gBRCA mutations in high grade, serous, epithelial ovarian cancer, fallopian tube cancer or primary peritoneal cancer.[16]

NICE currently recommend the following maintenance treatments for relapsed, platinum-sensitive ovarian cancer, fallopian tube cancer and primary peritoneal cancer:[16]

- Olaparib
- Rucaparib
- Niraparib

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Clinical Trial Information

Trial	**OPINION,** NCT03402841**;** A Phase IIIb, Single-arm, Open-label Multicentre Study of Olaparib Maintenance Monotherapy in Platinum-sensitive Relapsed Non-Germline BRCA Mutated Ovarian Cancer Patients Who Are in Complete or Partial Response Following Platinum Based Chemotherapy **Phase III –** active, not recruiting **Locations:** 13 EU countries, UK, Canada and other countries **Primary completion date:** October 2020
Trial Design	Single group assignment, open-label
Population	N=279; female adults aged 18 to 95 years with relapsed high grade serous ovarian cancer (including primary peritoneal and/or fallopian tube cancer) or high grade endometrioid ovarian cancer; patients must have completed at least 2 previous courses of platinum containing therapy
Intervention(s)	Olaparib (oral) 300mg twice daily
Comparator(s)	No comparator
Outcome(s)	Primary outcome measure: Progression free survival (PFS) [Time frame: up to maximum of 32 months] See trial record for a full list of other outcomes
Results (efficacy)	Median PFS was 9.2 months (95% CI 7.6-10.9) with 210 PFS events (75.3% maturity). 65.3%, 38.5% and 24.3% of patients were progression-free at 6, 12 and 18 months respectively.[3]
Results (safety)	Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 29% of patients and serious TEAEs occurred in 19.7% of patients. TEAEs led to dose interruption, dose reduction and treatment discontinuation in 47%, 22.6% and 7.5% of patients respectively.[3]

Estimated Cost

Olaparib is already marketed in the UK for various indications; a pack of 56 x 100mg and 56 x 150mg tablets costs £2317.50 and a pack of 448 x 50mg capsules costs £3550.00.[17]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Olaparib plus bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer (TA693). April 2021.
- NICE technology appraisal. Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy (TA673). February 2021.
- NICE technology appraisal. Olaparib for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian tube or peritoneal cancer (TA620). January 2020.

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- NICE technology appraisal. Rucaparib for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian tube or peritoneal cancer (TA611). November 2019.
- NICE technology appraisal. Olaparib for maintenance treatment for BRCA mutation-positive advanced ovarian, fallopian tube or peritoneal cancer after response to first-line platinum-based chemotherapy (TA598). August 2019.
- NICE technology appraisal. Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer (TA528). July 2018.
- NICE clinical guideline. Ovarian cancer: recognition and initial management (CG122). April 2011.
- NICE quality standard. Ovarian cancer (QS18). May 2012.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract For Complex Gynaecology – Specialist Gynaecological Cancers. E10/S/f.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Other Guidance

- Armstrong DK, Alvarez RD, Bakkum-Gamez JN, Barroilhet L, Behbakht K et al. Ovarian Cancer Version 2. 2020, NCCN Clinical Practice Guidelines in Oncology. February 2021.[18]
- Fotopoulou C, Hall M, Cruickshank D, Gabra H, Ganesan R et al. British Gynaecological Cancer Society (BGCS) epithelial ovarian/fallopian tube/primary peritoneal cancer guidelines: recommendations for practice. June 2017.[19]
- Scottish Intercollegiate Guidelines Network. SIGN 135 – Management of epithelial ovarian cancer. November 2013.[20]

Additional Information

AstraZeneca did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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