Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2209

olaparib 100mg and 150mg film-coated tablets (Lynparza®)

AstraZeneca UK Limited.

8 November 2019

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission considered under the orphan equivalent process

olaparib (Lynparza®) is accepted for use within NHSScotland.

Indication under review: for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) BRCA1/2-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.

In a phase III study, olaparib prolonged progression-free survival compared with placebo.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a list price that is equivalent or lower.

This advice takes account of views from a Patient and Clinician Engagement (PACE) meeting.

Chairman
Scottish Medicines Consortium

Indication

Olaparib monotherapy is indicated for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) BRCA1/2-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.[1]

Dosing Information

The recommended dose of olaparib is 300mg (two 150mg tablets) orally taken twice daily, equivalent to a total daily dose of 600mg. The 100mg tablet is available for dose reduction. Olaparib tablets should be swallowed whole and not chewed, crushed, dissolved or divided. Olaparib tablets may be taken without regard to meals.

Patients with platinum-sensitive high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy should start treatment with olaparib no later than 8 weeks after completion of their final dose of the platinum-containing regimen.
Patients can continue treatment until radiological disease progression, unacceptable toxicity or for up to 2 years if there is no radiological evidence of disease after 2 years of treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating physician can derive further benefit from continuous treatment, can be treated beyond 2 years.
Olaparib tablets (100mg and 150mg) should not be substituted for olaparib capsules (50mg) on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation. Therefore, the specific dose recommendations for each formulation should be followed.
See summary of product characteristics for dose adjustments for adverse reactions, renal impairment and for co-administration with CYP3A inhibitors.
Treatment with olaparib should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.[1]

Product availability date

12 June 2019
Olaparib meets SMC orphan equivalent criteria for this indication.

Summary of evidence on comparative efficacy

Olaparib inhibits human poly (ADP-ribose) polymerase enzymes (PARP1, 2 and 3) and has been shown to inhibit tumour growth and cause cancer cell death. PARP enzymes play a role in the efficient repair of DNA single strand breaks.[1] Olaparib is the first PARP inhibitor to be licensed as maintenance treatment for the indication under review. Olaparib 50mg hard capsules are already accepted for use in NHSScotland as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous

epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy (SMC 1047/15). The current submission is for use earlier in the disease pathway after first line platinum therapy.

The key evidence to support the efficacy and safety of olaparib as maintenance therapy in adult patients with newly diagnosed, histologically confirmed advanced (FIGO stage III or IV), BRCA mutated, high grade serous or endometrioid ovarian cancer, primary peritoneal cancer, or fallopian-tube cancer comes from SOLO1, a randomised, double-blind, placebo-controlled, international, phase III study.[2, 3] Patients were required to have undergone either biopsy (stage IV disease only), an attempt at cytoreductive surgery before the start of chemotherapy (up front surgery) or cytoreductive surgery while completing a chemotherapy treatment (interval surgery); have a deleterious or suspected deleterious germline BRCA1/2 mutation; received 6 to 9 cycles of platinum-based chemotherapy without bevacizumab, or a minimum of 4 cycles if treatment was discontinued due to toxicities, and have a complete clinical response (no evidence of disease on imaging and a normal CA-125 level) or a partial clinical response (a ≥30% decrease in tumour volume from the start to the end of chemotherapy or no evidence of disease on imaging after chemotherapy but a CA-125 level above the upper limit of the normal range). Patients had an Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1, normal organ and bone-marrow function.[3]

Following completion of platinum-based chemotherapy, patients were centrally randomised, in a 2:1 ratio to receive olaparib 300mg orally twice daily or placebo. Randomisation was stratified according to clinical response after platinum-based chemotherapy (complete or partial).[3] Patients were randomised within 8 weeks of their last dose of chemotherapy.[2] Study treatment was continued until investigator-assessed objective disease progression, based on modified Response Evaluation Criteria in Solid Tumours [RECIST], version 1.1, provided the patient was deriving clinical benefit and did not meet any discontinuation criteria. Patients who had no evidence of disease at 2 years stopped receiving study treatment, but patients who had a partial response at 2 years were allowed to continue receiving blinded study treatment. Following discontinuation of the study treatment, patients could receive treatments at the investigators' discretion.[3]

The primary outcome was progression-free survival (PFS), defined as the time from randomisation until the date of investigator-assessed objective disease progression according to RECIST v1.1 or death, in the intention-to-treat population, which included all randomised patients . Patients who had not progressed or died at the time of analysis were censored at the time of their last evaluable assessment.[2, 3] At the time of the primary analysis 198 PFS events had occurred and the median follow-up time was 41 months in both groups.[2, 3] Detailed results are described in Table 1.

Table 1. Progression-free survival for treatment groups of SOLO1 study.[2]

		Olaparib (n=260)	Placebo (n=131)
Progression-free survival	Number of events	102	96
	Median time	NR	13.8 months
	HR (95% CI)	0.30 (0.23 to 0.41), p<0.001	
	KM 3-year rate	60%	27%

NR = not reached, HR = hazard ratio, CI = confidence interval; KM = Kaplan-Meier estimate.

The key secondary outcomes, time from randomisation to second progression (PFS2) and overall survival were controlled for multiplicity using a hierarchical testing strategy. The first key secondary outcome tested was PFS2, defined as the time from the date of randomisation to the earliest progression event assessed by investigator (based on radiological, CA-125 or symptomatic progression) or death, subsequent to the PFS event used for the primary analysis.[2] At the time of the primary analysis 121 PFS2 events had been reported with median follow-up times of 41 and 38 months for the olaparib and placebo groups respectively.[2, 3] Overall survival (time from randomisation until death) data were immature at the time of the primary analysis. Results are presented in Table 2.

Table 2. Key secondary outcomes of SOLO1 study.[2, 3]

		Olaparib (n=260)	Placebo (n=131)
Time from randomisation to second progression	Number of events	69	52
	Median time	NR	41.9 months
	HR (95% CI)	0.50 (0.35 to 0.72), p<0.001	
	KM 3-year rate	75%	60%
Overall survival	Number of events	55	27
	Median time	NR	NR
	HR (95% CI)	0.95 (0.60 to 1.53)	
	KM 3-year rate	84%	80%

NR = not reached, HR = hazard ratio, CI = confidence interval; KM = Kaplan-Meier estimate.

The results of other secondary outcomes including time from randomisation to: study treatment discontinuation or death, start of first subsequent therapy or death and start of second subsequent therapy or death, were all in line with the primary analysis of PFS.[2]

The blinded independent central review analysis of PFS was consistent with the primary investigator-assessed analysis, with hazard ratio of 0.28 (95% confidence interval [CI]: 0.20 to 0.39). In the olaparib and placebo groups median PFS was not reached versus 14.1 months and Kaplan-Meier estimated 3-year PFS was 69% versus 35%, respectively.[3] Sensitivity analyses to

evaluate attrition bias, evaluation time bias and possible informative censoring were all consistent with the primary analysis.[3]

Subgroup analyses of PFS based on the following subgroups were all in-line with the primary analysis: clinical response after chemotherapy (complete or partial), ECOG performance status (0 or 1), CA-125 level at baseline (> or ≤ ULN), germline BRCA mutation (BRCA1, BRCA2, BRCA1 and BRCA2, or none), age (< or ≥65 years), FIGO stage at diagnosis (stage III or IV) and presence of residual macroscopic disease after debulking surgery performed prior to study entry (yes or no). [3]

Health-Related Quality of Life (HRQoL) was assessed by the Functional Assessment of Cancer Therapy - Ovarian (FACT-O) questionnaire and the Trial Outcome Index (TOI) of FACT-O as exploratory outcomes. The analysis of the change from baseline in TOI scores for the first 24 months of treatment was added as a protocol amendment while the study was ongoing. There was a nominal reduction in TOI scores, suggesting a decrease in quality of life, associated with olaparib compared with placebo.[2-4]

Summary of evidence on comparative safety

The safety profile of olaparib in SOLO1 was generally consistent with its known safety profile, with adverse events (AEs) mostly of mild or moderate severity.[2] Safety analyses were conducted in the safety population, which included all patients who received at least one dose of study treatment.[3] The proportions of patients in the olaparib (n=260) and placebo (n=130) groups with any AE were 98% and 92%, any serious AE were 21% and 12% (anaemia was the most common AE, accounting for 6.5% and 0%), an AE leading to treatment discontinuation were 12% and 2.3%, an AE leading to treatment interruption were 49% and 16%, and an AE leading to a dose reduction were 29% and 3.8%. Excluding dose interruptions, the mean actual treatment exposure time in the olaparib and placebo groups were 87 weeks and 65 weeks respectively.[2]

For the olaparib and placebo groups the following AEs of any grade were reported: nausea (77% and 38%), fatigue (41% and 30%), vomiting (40% and 15%), anaemia (39% and 10%) diarrhoea (34% and 25%), constipation (28% and 19%), dysgeusia (altered taste sensation) (26% and 3.8%), asthenia (24% and 12%), neutropenia (23% and 12%), dyspnoea (15% and 5.4%), urinary tract infection (12% and 6.2%) thrombocytopenia (11% and 3.8%), and lymphopenia (6.2% and 1.5%).[2, 3]

Summary of clinical effectiveness issues

The early stages of ovarian cancer tend to be asymptomatic or associated with non-specific symptoms. As a result it is detected at an advanced stage approximately 75% of the time.[2, 5] Mutation of the breast cancer susceptibility genes (BRCA1/2) increases an individual's risk of developing cancers, especially ovarian or breast cancer, and approximately 25% of patients with high grade serous ovarian cancer have a BRCA mutation.[6] Women with BRCA mutations are more

likely to develop ovarian cancer at a younger age and have platinum-sensitive disease than ovarian cancer patients without a BRCA mutation.[7, 8] Cytoreductive surgery and platinum-based chemotherapy (such as carboplatin plus paclitaxel) are usually first line treatment for advanced disease. Women who respond to chemotherapy are monitored for disease progression (which occurs in approximately 75% of patients) and then considered for a subsequent course of chemotherapy on progression. Bevacizumab in addition to carboplatin and paclitaxel, followed by continued bevacizumab monotherapy, is a front-line treatment option for patients with FIGO stage IV disease (SMC806/12). Women with relapsed disease who are at least partially platinum-sensitive (progression following an interval >6 months after previous platinum-chemotherapy) are offered a further course of platinum-based chemotherapy. Patients with BRCA mutations who respond to the second-line of chemotherapy are managed with active surveillance, or with olaparib (SMC 1047/15).[5, 9, 10] Olaparib meets SMC orphan-equivalent criteria for this indication.

The primary PFS analysis of SOLO1 demonstrated use of olaparib, as maintenance treatment following completion of first line platinum-based chemotherapy, was associated with a clinically significant improvement in PFS when compared with placebo (that is, active surveillance). Olaparib extended PFS with a HR of 0.30 and prolongs PFS2, with a HR of 0.50. However, overall survival data were immature at the time of analysis.[2, 3]

The PFS2 analysis data were not mature and likely over-represent patients with a short-lasting response to first-line treatment due to poor platinum sensitivity. Additionally, PFS2 might also have been influenced by inclusion of the biomarker CA-125 as a criterion for disease progression. CA-125 was not included in the criteria for a PFS event.[2] Overall survival data are immature and subsequent lines of therapy are likely to affect the interpretation of the final overall survival analysis. Within the olaparib and placebo groups 7.7% (20/260) and 37% (49/131), respectively, received subsequent treatment that included a PARP inhibitor, with 5.0% and 34% receiving olaparib.[2]

The HRQoL analysis has limitations which make interpretation of the results uncertain. Olaparib was associated with an almost 20% higher incidence of anaemia of grade 3 or higher than patients treated with placebo. This may impact on patients' quality of life, however prolonging time to another line of chemotherapy may maintain quality of life for longer in patients treated with olaparib.

Patients with somatic BRCA mutations or non-serous histology accounted for small proportions (≤5%) of patients in the SOLO1 study. Olaparib effects in these groups are uncertain due to the small number of patients. The European Medicines Agency considered that similar effectiveness would be expected in patients with somatic and germline BRCA mutations, and in patients with serous and non-serous histology.[2]

The study excluded patients with ECOG performance status of 2 or greater, which may affect the application of the results to less fit patients. The study excluded patients who had been diagnosed

and treated for earlier stages of the disease and patients who had more than one debulking surgery. This may affect the application of results to these patient groups.

Placebo is the relevant comparator for patients with stage III disease as these patients are currently managed with active surveillance following a response to platinum-based chemotherapy. Patients with stage IV disease may be treated with bevacizumab in combination with carboplatin and paclitaxel chemotherapy for up to 6 cycles followed by continued use of single agent bevacizumab until disease progression or for a maximum of 15 months.

Clinical experts consulted by SMC considered that olaparib is a therapeutic advancement due to benefits in PFS and because it provides a licensed maintenance therapy for these patients, particularly for patients with stage III disease, as the platinum based chemotherapy plus bevacizumab regimen for first-line therapy is not recommended in this patient group.

*Other data were also assessed but remain confidential.**

Patient and clinician engagement (PACE)

- Advanced ovarian cancer usually responds to first-line chemotherapy treatment, but recurrence is common (>70%) and relapsed disease is incurable. Patients with stage IV disease can receive bevacizumab maintenance therapy, but there are no licensed maintenance therapies for stage III disease and patients have only active surveillance. During this time the majority of patients endure severe anxiety about recurrence, which has been described as living with a “ticking time bomb”.
- First-line treatment of advanced ovarian cancer provides the only opportunity for cure. There is an urgent unmet need for effective maintenance treatments that increase the proportion of patients achieving cure or that delay relapse and that are convenient and do not have a negative impact on quality of life.
- Olaparib maintenance therapy, compared with placebo, increases progression free survival substantially and, although overall survival data are immature, expert clinicians believe that olaparib may have the potential to improve overall survival and increase the proportion of patients who achieve cure or a long-lasting remission. Olaparib is convenient to administer and its adverse events are considered manageable.
- Olaparib would markedly reduce the anxiety that patients and their family experience after first-line chemotherapy and give them hope that long-term remission of cure may be possible.
- By increasing the time to recurrence olaparib would give the patient more time when they are generally well and able to maintain family and work commitments. This may be have particular relevance in patients with BRCA1/2-mutations, who are typically younger and more likely to have work and family responsibilities for young children. Patients and their carers

would also be spared the strain associated with repeated courses of chemotherapy which have significant cumulative toxicities and require numerous visits to hospital.

- The increase in progression free survival with olaparib is greater when it is used in the first-line setting compared with the second-line setting. Also, as recurrent disease may be less likely to respond to platinum-based chemotherapy, the number of patients able to access olaparib in the second-line setting would be lower than in the first-line setting. Using olaparib in the first-line setting would optimise the benefits that can be obtained from this medicine for patients with advanced ovarian cancer.

Additional Patient and Carer Involvement

We received patient group submissions from: Ovacome Ovarian Cancer Charity, Ovarian Cancer Action and Target Ovarian Cancer. Ovarian Cancer Action and Target Ovarian Cancer are both registered charities and Ovacome Ovarian Cancer Charity is a Charitable Incorporated Organisation. In the past two years, Ovarian Cancer Action has received less than 1% pharmaceutical company funding and Ovacome Ovarian Cancer Charity has received 1.58% pharmaceutical company funding, both including from the submitting company. Target Ovarian Cancer has received 2% pharmaceutical company funding in the past two years, with none from the submitting company. Representatives from all three organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

Summary of comparative health economic evidence

The company submitted a cost-utility analysis of olaparib monotherapy for the maintenance treatment of adult patients with newly diagnosed advanced (FIGO stages III and IV) BRCA1/2-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. The comparator was routine surveillance, which included patient observation, follow-up and general supportive or symptomatic care. SMC clinical expert responses confirm there is no active maintenance treatment for these patients.

A three-state partitioned survival model was presented consisting of three health states: progression-free (after response to first-line chemotherapy), progressed disease and death. A lifetime horizon was used which equated to 50 years in the base case analysis. This was reduced to 3040 years in the sensitivity analysis.

The clinical evidence to support olaparib came from the SOLO1 study described above. The company considered extrapolation of the entire SOLO1 study dataset would yield 'implausible' estimates of long-term survival. Instead, KM data were used directly until 24 months and then models were fitted to the post-24 month data in order to extrapolate over the model lifetime. This approach was said to have the benefit of excluding survival data from patients with early progression (that is PFS <2 years). For PFS, goodness of fit statistics, visual inspection and face-validity of the survival estimates were examined and based on this the log-normal parametric

model was selected for both arms to extrapolate data until 7 years. This time point was selected based on expert opinion that patients who remain progression-free beyond 5 to 10 years after diagnosis would be considered long-term survivors and at low risk of mortality. Beyond 7 years, an excess mortality rate of 1.26 was applied in the model to capture all-cause mortality rates for people with BRCA mutation who have no evidence of cancer.

A similar piecewise approach was taken to extrapolate overall survival data in the olaparib arm. To maintain consistency with the PFS analysis, KM data were used until 24 months and then the log-logistic model was used to extrapolate the post-24 month data in the olaparib arm. However, for the routine surveillance arm the company argued using the piecewise model approach would produce unrealistic estimates. The shape of the placebo overall survival KM curve in the SOLO1 study showed a flattening of the curve from month 30 suggesting a low risk of death for routine surveillance in practice. This was said to be clinically implausible based on current 5-year survival data and estimates from the Edinburgh Ovarian Cancer Database. As a result, an alternative approach was used in the routine surveillance arm to extrapolate beyond the 2 year KM data. This involved using the survival models fitted to the olaparib arm for overall survival but adjusting them using a constant treatment effect to account for the assumed poorer longer-term survival in the routine surveillance arm. This treatment effect was not estimated using the overall survival data from the SOLO1 study, but instead the difference in survival was estimated based on the difference observed in the PFS2 secondary endpoint (time from randomisation to second progression) used as a surrogate for overall survival. Justification for this approach was provided using data from a separate olaparib study (Study 19) where time to subsequent therapy (TSST), a surrogate endpoint for PFS2, showed similar gains in median TSST and median overall survival with olaparib. PFS2 data from SOLO1 were extrapolated which resulted in a predicted gain in median overall survival with olaparib.

Quality of life data were collected in SOLO1 using EQ-5D-5L. These data were mapped to EQ-5D-3L for the base case analysis, with EQ-5D-5L used in sensitivity analysis. Data were pooled across the treatment groups to produce utility values in the PFS and progressed disease health states. Age-related adjustments were made to the utility values over time. Disutilities due to adverse events were applied as one-off decrements applied to patients experiencing anaemia, neutropenia, and diarrhoea using the rates observed in SOLO1.

Costs included medicine acquisition, administration, health state resource use, adverse events and end-of-life palliative care costs. Time to treatment discontinuation data were used to estimate treatment duration and the base case included treatment duration of longer than 2 years in 10% of patients.

BRCA testing costs were included in a scenario analysis. Subsequent treatments included olaparib capsules and chemotherapy based on the proportions who received these treatments in the SOLO1 study combined with data on the duration of subsequent treatment in a second-line or later setting. A proportion of patients in the olaparib arm received subsequent PARP inhibitor treatment in SOLO1 but the cost of this was excluded from the olaparib arm on the basis that patients would not receive re-treatment with olaparib in practice and no other PARP inhibitors are approved for use in Scotland.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. The results of the base case analysis and selected sensitivity analysis are presented in tables 1 and 2 below.

The incremental cost associated with olaparib is largely driven by the medicine acquisition cost of olaparib and the majority of the QALY gain is due to the predicted increased time in the progression-free health state.

Table 3: Base case results with PAS

	ICER (£/QALY)
Olaparib tablets versus routine surveillance	£22,748

LYG = life-years gained, QALYs = quality-adjusted life-years, ICER = incremental cost-effectiveness ratio

Table 4: Selected sensitivity analysis results

	Scenario	**ICER (£/QALY) with PAS**
1	Time horizon reduced to 40 years	£22,888
2	Time horizon reduced to 30 years	£25,016
3	Fully parametric model using best fitting distributions (PFS = generalised gamma, OS = loglogistic).	£25,533
4	Long term relapse free survival cut-off increased to 10 years (7 in base case)	£26,570
5	Patients surviving beyond 7 years assumed cured (i.e. mortality rate = 1 instead of 1.26)	£21,884
6	Inclusion of BRCA testing costs	£23,364
7	PFS: OS ratio= 1:0.5	£27,850
8	Alternative PFS extrapolation approach: Weibull	£25,961
9	Alternative OS extrapolation approach for olaparib: Lognormal	£33,992
10	OS modelling of olaparib: 36 months of KM data used rather than 24	£24,091
11	No treatment beyond 2 years	£19,352

ICER = Incremental cost-effectiveness ratio, TTD = time to treatment discontinuation, PFS = progression-free survival. HR = hazard ratio OS= Overall survival

The following limitations were noted and largely relate to the modelling of the predicted overall survival gains in the model:

- Overall survival data from SOLO1 are immature with median survival not yet reached in either arm. The KM curves show separation of the curves with improved survival in the olaparib arm until around 30 months but followed by convergence of the curves by around 40 months. While the gain in PFS with olaparib demonstrated in SOLO1 is significant and suggestive of an overall survival benefit, the magnitude of this benefit is uncertain. As shown in sensitivity

analysis, the results were sensitive to assuming a less optimistic relationship between PFS and OS than was modelled in the base case.

- The placebo overall survival data were not used in the model to estimate survival in the routine surveillance arm. The company argued that the KM estimates of overall survival in SOLO1 were implausible and would produce unrealistic long-term estimates of survival. Comparisons with real-world data were provided to further justify not using these data directly in the model. However, there are limitations with the real-world data and concerns the SOLO1 data have not be used in the model extrapolations given they are likely to provide the most robust basis for extrapolation.
- As noted, instead of using overall survival data from the placebo arm, the company used a particularly complicated approach which involved several assumptions and used data from other studies to validate the approach used. The estimates of overall survival based on this approach are particularly uncertain. While there may be limitations with using the overall survival data from the placebo arm in a conventional way, it would be helpful to have further explored using these data in some form in the model. For example, given the main concern relates to the placebo data from month 30 onwards, the data up to a particular time point could have been used to provide long-term estimates of survival. The company was asked to comment on this but did not provide any results exploring an alternative approach.
- Given the complexities involved in the overall survival predictions and immaturity of the overall survival estimates in the model, the sensitivity analysis provided to test this aspect of the model was limited. Additional sensitivity analysis was provided as shown in sensitivity analyses 7 to 10 and shows upward movement in the ICERs from the use of alternative data or methods to estimate treatment benefits.

The Committee also considered the benefits of olaparib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for the absence of other treatments of proven benefit was satisfied. In addition, as olaparib is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence, the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee accepted olaparib for use in NHSScotland.

*Other data were also assessed but remain confidential.**

Additional information: guidelines and protocols

The European Society for Medical Oncology (ESMO) and European Society of Gynaecological Oncology (ESGO) published consensus conference recommendations on ovarian cancer in May 2019.[10] The recommendations include:

- 3-weekly carboplatin/paclitaxel remains the standard-of-care chemotherapy of first-line ovarian cancer treatment

- Bevacizumab could be considered in addition to carboplatin and paclitaxel in patients with stage III/IV ovarian cancer
- PARP inhibitors (olaparib, niraparib and rucaparib) may be given as maintenance therapy following a response to platinum-based second or higher line of treatment as there is proven benefit with respect to PFS. The benefit is greatest in patients with a BRCA mutation.
- PARP inhibitors could be considered as monotherapy in patients with a BRCA mutation
- The recommended length of treatment with PARP inhibitors remains unclear as the benefit of continuing treatment beyond progression has not been demonstrated conclusively at this point.

The Scottish Intercollegiate Guidelines Network (SIGN) published SIGN 135: Management of epithelial ovarian cancer in November 2013 and published a revised version in 2018. Recommendations are broadly in line with the ESMO and ECGO recommendations.[5]

The British Gynaecological Cancer Society published epithelial ovarian / fallopian tube / primary peritoneal cancer guidelines: recommendations for practice in 2017. They note that treatment with a PARP inhibitor may offer longer-term remission and response for some *BRCA*-mutation carriers.[11]

Additional information: comparators

Routine surveillance

Cost of relevant comparators

Medicine	Dose Regimen	Cost per year (£)
Olaparib film-coated tablets	**300mg oral twice daily**	**60,255**

Costs from BNF online on 25 July 2019.

Additional information: budget impact

The company estimated 40 patients would be eligible for treatment in year 1 rising to 62 patients in year 5. The estimated uptake rates were 75% (22 patients) in year 1 and 84% (52 patients) in year 5. A discontinuation rate of 26% was assumed.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 13 September 2019.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are

therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.