

Chemotherapy Protocol
GYNAECOLOGICAL CANCERS

OLAPARIB (tablets)

This regimen may require funding.

Regimen

- Ovarian Cancer – Olaparib (tablets)

Indication

- Olaparib in its tablet formulation is recommended as maintenance treatment in patients with high grade epithelial stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based FIRST line chemotherapy AND who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation where the following criteria are met:
 - the patient has a proven histological diagnosis of predominantly high grade serous or endometrioid ovarian, fallopian tube or primary peritoneal carcinoma.
 - the patient has a documented deleterious or suspected deleterious BRCA 1 or BRCA 2 mutation(s).
 - the patient has recently diagnosed FIGO stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma. Maintenance olaparib is not funded for patients with recently diagnosed and treated stage 1-IIIC disease or for patients relapsing after previous treatment.
 - one of the following scenarios applies to the surgical management of the patient in relation to the stage of the disease:
 - (a) the patient has stage III disease and had an upfront attempt at optimal cytoreductive surgery or
 - (b) the patient has stage III disease and had an interval attempt at optimal cytoreductive surgery or
 - (c) the patient has stage IV disease and had an upfront attempt at optimal cytoreductive surgery or
 - (d) the patient has stage IV disease and had an interval attempt at optimal cytoreductive surgery or
 - (e) the patient has stage IV disease and has had a biopsy only
 - the patient has been treated with platinum-based 1st line chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.
 - the patient is currently less than 8 weeks from the date of the last infusion of the last cycle of 1st line chemotherapy unless the patient was entered into the company's early access scheme for maintenance olaparib after 1st line chemotherapy
 - that the patient has responded to the recently completed 1st line chemotherapy and has achieved a partial or complete response to treatment according to the definitions given below and with no evidence of progressive disease on the post-treatment scan or a rising CA125 level.
 - (a) achieved a complete response at the end of 1st line chemotherapy ie has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal or
 - (b) achieved a partial response at the end of 1st line chemotherapy ie has had a $\geq 30\%$ reduction in measurable or non-measurable disease from the start of to the

- completion of 1st line chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range.
- that the patient has not previously received any PARP inhibitor (unless previously enrolled in the company's early access scheme for maintenance olaparib after 1st line chemotherapy).
- that olaparib will be used as monotherapy and not administered concurrently with maintenance bevacizumab.

- Olaparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment or for total treatment duration of 2 years if the patient is in complete remission at the end of the 2 year treatment period. For those patients with stable residual disease after completing 2 years of treatment, treatment with maintenance olaparib can continue if the treating clinician considers that the patient will derive further benefit. If treatment beyond 2 years is to occur, CDF form OLAP1b must be completed prior to continuation otherwise olaparib will not be funded by the CDF.
- Performance status 0, 1 (a patient with a performance status of 2 or more is not eligible for olaparib)
- A formal medical review as to whether maintenance treatment with olaparib should continue or not will be scheduled to occur at least by the start of the third cycle of treatment
- No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve)
- Olaparib in its tablet formulation is to be otherwise used as set out in its Summary of Product Characteristics

Toxicity

Drug	Adverse Effect
Olaparib	AML, pneumonitis, reduced appetite, nausea and vomiting, headache, dysgeusia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- BRCA testing prior to starting therapy
- FBC, U&Es, creatinine, LFTs monthly for the first twelve months then 2-3 monthly thereafter
- CA125 where appropriate

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped. Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Eligible levels should be;

Test	Level
Neutrophils	Greater than $1 \times 10^9/L$
Platelets	Greater than $100 \times 10^9/L$

If a patient develops severe haematological toxicity or blood transfusion dependence, treatment with olaparib should be interrupted and appropriate haematological testing initiated. If the blood parameters remain clinically abnormal after four weeks of olaparib dose interruption bone marrow analysis and / or blood cytogenetic analysis are recommended.

Hepatic Impairment

The SPC does not recommend dose modifications for patients with Child Pugh A or B hepatic impairment and states that there are no data for use in Child Pugh C hepatic impairment. Therefore, olaparib is not recommended for use in patients with Child Pugh C hepatic impairment.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Olaparib	More than 50	100%
	31 to 50	200mg twice daily
	Less than 31	No information available. Only use if the benefits outweigh the risk

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes. Dose interruption can be considered. If dose reduction is thought appropriate then the dose should be reduced from 300mg twice a day to 250mg twice a day. If a further reduction is necessary then prescribe 200mg twice a day.

Myelodysplastic Syndrome / Acute Myeloid Leukaemia

Myelodysplastic syndrome / Acute Myeloid Leukaemia (MDS/AML) have been reported in a small number of patients who received olaparib alone or in combination with other anti-cancer drugs; the majority of cases have been fatal. The duration of therapy with olaparib in

patients who developed MDS/AML varied from less than 6 months to more than 2 years. The cases were typical of secondary MDS/cancer therapy-related AML. All patients had potential contributing factors for the development of MDS/AML; the majority of cases were in *gBRCA* mutation carriers and some of the patients had a history of previous cancer or of bone marrow dysplasia. All had received previous platinum- containing chemotherapy regimens and many had also received other DNA damaging agents and radiotherapy. If MDS and/or AML are confirmed while on treatment with olaparib, it is recommended that the patient be treated appropriately. If additional anticancer therapy is recommended, olaparib should be discontinued and not given in combination with other anticancer therapy.

[Pneumonitis](#)

Pneumonitis has been reported in a small number of patients receiving olaparib, and some reports have been fatal. The reports of pneumonitis had no consistent clinical pattern and were confounded by a number of pre-disposing factors (cancer and / or metastases in lungs, underlying pulmonary disease, smoking history, and / or previous chemotherapy and radiotherapy). If patients present with new or worsening respiratory symptoms such as dyspnoea, cough and fever, or a radiological abnormality occurs, olaparib treatment should be interrupted and prompt investigation initiated. If pneumonitis is confirmed, olaparib treatment should be discontinued and the patient treated appropriately.

[Embryofaetal Toxicity](#)

Based on its mechanism of action (PARP inhibition), olaparib could cause foetal harm when administered to a pregnant woman. Nonclinical studies in rats have shown that olaparib causes adverse effects on embryofaetal survival and induces major foetal malformations at exposures below those expected at the recommended human dose of 300 mg twice daily. Olaparib should not be used during pregnancy and in women of childbearing potential not using reliable contraception during therapy and for 1 month after receiving the last dose of olaparib.

[Regimen](#)

28 day cycle until disease progression or unacceptable toxicity occurs (24 cycles will be set in Aria)

Treatment should be commenced no more than eight weeks after completion of the last cycle of platinum based chemotherapy.

Drug	Dose	Days	Administration
Olaparib	300mg twice a day	Continuous	Oral

[Dose Information](#)

- Olaparib is available as 100mg and 150mg tablets
- Olaparib is also available as 50mg hard capsules. The capsules are not bioequivalent with the tablets and the doses are different. The tablets and capsules are not interchangeable

- Doses will be rounded to the nearest 50mg (up if halfway)

Administration Information

- If a dose is missed, the next dose should be taken at its scheduled time.

Additional Therapy

- No routine supportive medication is required

Additional Information

- The National Patient Safety Alert on oral SACT (NPSA/2008/RRR001) must be followed in relation to olaparib.
- It must be made clear to all staff, including those in the community, that olaparib should only be prescribed under the supervision of an oncologist.
- Olaparib interacts with many other agents. Always check for drug interactions.

Coding

- Procurement – X71.5
- Delivery – X73.1

References

1. National Institute for Health and Clinical Excellence (2016). 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. Technology appraisal guidance TA381. DOH:London

REGIMEN SUMMARY

Olaparib (tablets)

Cycle 1 onwards

Take Home Medicines

1. Olaparib 300mg twice a day oral

Administration Instructions
Oral SACT

Olaparib tablets should be swallowed whole and not chewed, crushed, dissolved or divided. Olaparib tablets may be taken without regard to meals

Olaparib tablets should not be substituted for olaparib capsules 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. Please refer to the SPC.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Sept 2019	None	Dr Deborah Wright Pharmacist	Dr C Green Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.